# Novel Foods and Food Allergy

## An exploratory study of novel foods as allergy management strategy

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This research was conducted under the auspices of the Mansholt Graduate School for Social Sciences (MG3S)

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## An exploratory study of novel foods as allergy management strategy

**Margreet C. van Putten**

**Thesis**
submitted in partial fulfilment of the requirements for the degree of doctor
at Wageningen University
by the authority of the Rector Magnificus
Prof. dr. M.J. Kropff,
in the presence of the
Thesis Committee appointed by the Doctorate Board
to be defended in public
on Tuesday 15 September
at 1.30 PM in the Aula.

Margreet C. van Putten
Novel Foods and Food allergies: an exploratory study of novel foods as allergy management strategy,
125 pages

Thesis, Wageningen University, Wageningen, NL (2009)
With references, with summaries in Dutch and English

ISBN: 978-90-8585-449-4

## Abstract

Food allergy represents an increasing concern to society. It is defined as an inappropriate immunological reaction to normally harmless food components and affects 5-8% of children and 1-2% of adults. Since at the time of writing no cure for food allergy exists, food allergic consumers need to avoid all problematic foods and ingredients, which may have a negative impact on the quality of life and economic functioning of food allergic consumers and their families. Food allergies may also result in substantial costs for society overall in terms of health care costs and absenteeism.

Novel foods are continuously being developed and introduced onto the European market. The novelty of a food can be the result of: (1) genetic modification (GM) of the food itself, or its production using genetically modified organisms, (2) the application of novel processing techniques, or (3) the food in question having no prior history of consumption in general, or in a specific region or country. One potential benefit of novel foods is that of hypoallergenicity, although there is the potential risk that new proteins are introduced into the human food chain together with the novel foods.

The aim of the research presented in this thesis is to investigate whether novel foods can be used as part of an allergy management strategy. The issues associated with novel foods and food allergy are identified and insight is gained in stakeholder and consumer attitudes towards the application of novel foods as allergy management strategy. In addition, the existing novel food legislation regarding novel foods is reviewed with respect to risks (and benefits) of novel foods associated with food allergy.

The results show that that although hypoallergenic novel foods can have some positive contribution to food allergy management, their influence remains limited because many other factors other than the available foods cause the food allergy problems.

Overall, this research contributes to a better understanding of the impact of food allergy on daily lives of food allergic consumers and shows that although hypoallergenic novel foods can facilitate allergen avoidance, their influence remains limited because many other factors, such as the recognition of their allergy by their social environment cause the food allergy problems. Nevertheless, considering that the food allergy management options are limited, the contribution that hypoallergenic novel foods, which can be replacement for allergenic foods may be valuable for consumers who are allergic to foods that are easy to recognise and avoid.

# Voorwoord

Na ruim vijf jaar is het moment aangebroken dat ik de laatste woorden voor dit proefschrift schrijf. Tijdens die vijf jaar heb ik vaak nagedacht over wie ik allemaal met welke woorden zou willen bedanken voor hun bijdrage aan dit proefschrift. Nu ik het op wil schrijven klinken de meeste woorden te cliché en dekken ze de lading niet goed genoeg. Dit proefschrift zou er niet geweest zijn zonder de inbreng en ondersteuning van verschillende mensen. Het is onmogelijk om iedereen bij naam te noemen, dus hierbij wil ik iedereen die een bijdrage heeft geleverd aan dit proefschrift bedanken. Verscheidene mensen heb ik een eervolle vermelding in dit proefschrift beloofd als dank voor hun hulp en daarom ga ik hier proberen onder woorden te brengen hoe waardevol de verschillende bijdragen aan dit proefschrift voor mij zijn geweest.

First of all I would like to thank my promotor, Lynn Frewer for her advice and continuous support during these years. Your thoughts and suggestions helped me structuring the research. I found the discussions we had very useful and I always felt more motivated to complete this thesis after our meeting.

Mijn tweede promotor, Bart Gremmen wil ik bedanken voor zijn begeleiding en interesse tijdens dit onderzoek. Mede door jouw inzet en betrokkenheid heb ik dit proefschrift af kunnen schrijven. De gesprekken met jou en jouw kritische vragen hielden mij scherp, zodat ik nooit uit het oog verloor wat het doel van het onderzoek was.

Ook vanuit de bèta hoek heb ik ondersteuning gehad bij het schrijven van dit proefschrift. Luud Gilissen, Harry Wichers, Gijs Kleter en Ad Peijnenburg hebben een onmisbare rol gespeeld bij het opzetten en uitwerken van de bèta component van dit onderzoek. Dankzij jullie kon ik de uitdaging om gamma onderzoek aan te vullen met bèta onderzoek aangaan.

Naast de Wageningse inbreng was er ook de Groningse door Ewoud Dubois en Bertine Flokstra-de Blok die geholpen hebben het kwaliteit van leven deel van het onderzoek vorm te geven. Jullie suggesties hebben mij goed op weg geholpen, waarvoor mijn dank.

Ik ben alle MCB collega's dankbaar voor de fijne sfeer en stimulerende werkomgeving op de gangen. Er zijn een paar MCB mensen die ik op deze plaats speciaal wil noemen: Arnout Fischer en Ivo van der Lans hebben mij op weg geholpen bij de analyses van de resultaten en in de gaten gehouden of ik op de goede weg bleef. Ik heb veel van jullie geleerd. Thanks to Vladimir and Meike for making the dull afternoons non existent due to the highly interesting discussions we had, while sharing an office.

Ook gaat mijn dank uit naar de collega's van META. Ook al hoorde ik maar half bij META, de uitjes en etentjes waren er niet minder gezellig om.

Als AIO-5 van het Allergie Consortium Wageningen heb ik regelmatig geborreld met de andere ACW AIOs waarbij we onder andere de (on)mogelijkheden van gamma-bèta interactie in het onderzoek deelden. Jullie hebben allemaal een goed voorbeeld neergezet tijdens jullie promoties en ik hoop dat ik jullie goede voorbeelden kan volgen.

Zoals was beloofd ook een eervolle vermelding voor mijn schoonzus Maartje van Eerd. Bedankt voor het helpen schrijven van het informatieartikel over voedselallergie.

Lieve Petra, het is onmogelijk om goed te beschrijven wat je voor mij betekent. Behalve voor de concrete hulp die je gaf als tweede codeerder voor de ATLAS analyses en bij het vertalen van de vragenlijsten, ben ik je dankbaar voor de emotionele steun die je mij hebt gegeven. Jouw opbeurende gesprekken met koffie, thee of wijn hielpen me weer op weg als ik het onderzoek niet meer zag zitten.

Maaike bedankt voor je luisterende oor en interesse in mijn onderzoek. Door jou ben ik op een andere manier naar mijn onderzoek gaan kijken wat ertoe bijgedragen heeft dat het proefschrift eruit ziet, zoals het er nu uitziet.

Pap en mam, jullie hebben mij altijd gestimuleerd om het beste uit mezelf te halen. Dat heeft ertoe geleid dat ik dit proefschrift heb kunnen schrijven. Ik had dit niet kunnen doen als jullie niet altijd achter mij gestaan zouden hebben. Dank jullie wel voor jullie vertrouwen.

Joost, jij en ik zijn een team. Samen kunnen wij alles aan en zonder jou had ik nooit de rust gehad om dit proefschrift te schrijven.

Margreet van Eerd-van Putten

# Contents

# Chapter 1

# General introduction

Allergies are a serious health problem. Many research activities have focussed on the medical treatment of allergic patients. The Allergy Consortium Wageningen aims to increase and communicate knowledge about allergens and allergy prevention with the focus on “Strategies for allergy management”. The research presented in this thesis about ‘Novel foods and food allergy’ is part of the Allergy Consortium’s research program, which also includes research on ‘Allergens in the green environment’, ‘Allergens in the food production chain’, ‘The role of lifestyle factors in the development of food allergies’, and on ‘Celiac Disease’.

## 1.1 Food allergy

Food allergy is a complex disease, with genetic predisposition, environmental factors and exposure conditions all contributing to inter-individual differences in susceptibility. Figure 1 provides an overview of the classification of adverse reactions to food.

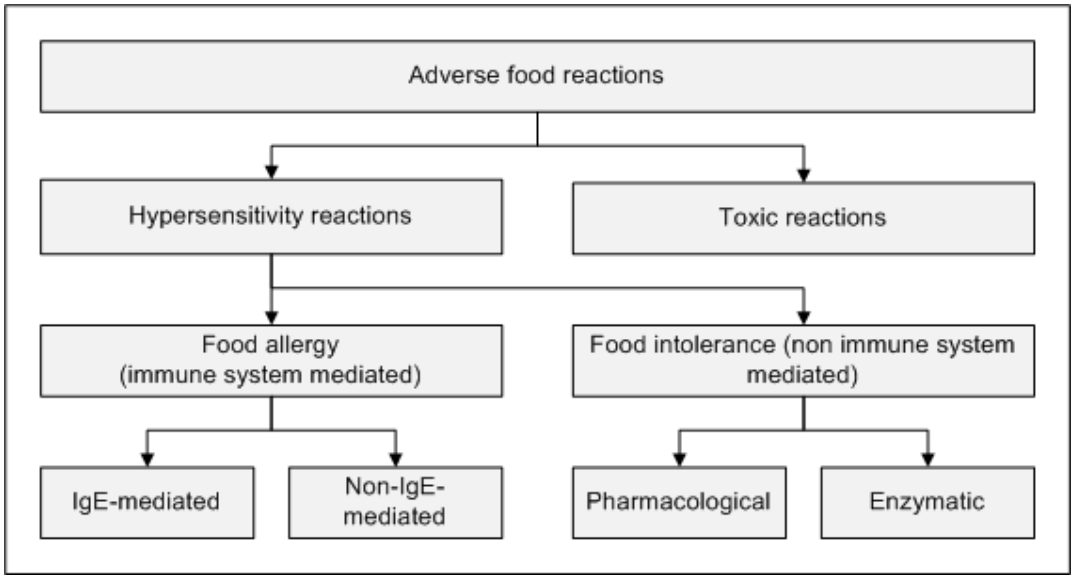


Figure 1.1: Classification of adverse food reactions (Patriarca et al., 2009).

Food allergy is defined as a hypersensitivity reaction that involves the immune system. Allergic reactions can be Immunoglobulin E (IgE) mediated, or non-IgE mediated. Examples of IgE mediated reactions are food and airway allergies. Examples

of non-IgE mediated reactions are celiac disease and contact dermatitis (Cox et al., 2007; Patriarca et al., 2009). Hypersensitivity reactions that do not involve the immune system are not considered as food allergies. Instead, these are called non- allergic food hypersensitivity, sometimes also referred to as food intolerance, which can be caused by pharmacologic, or enzymatic triggers (Patriarca et al., 2009).

True food allergy affects 5-8% of children and 1-2% of adults, although about 20% of people report an adverse reaction to food (Mills et al., 2007). The majority (approximately 90%) of food allergic reactions are caused by eight foods: milk, egg, peanuts, tree nuts, fish, soya, wheat and shellfish (Cox, 2008). Although controversy exists as to whether the prevalence of food allergy is increasing, it non-the-less remains an important health issue (Dearman and Kimber, 2009). Food allergy can also be the result of cross-reactivity, especially due to the high similarity of food proteins to inhalation allergens (e.g. from birch pollen or house dust mite). Apple allergy, with its widespread occurrence in North-West Europe, is a well-known example of a birch pollen related food allergy (Ferreira et al., 2004).

Food allergy diagnosis involves several steps. Skin prick testing with food extracts and with fresh foods, the measurement of food specific IgE, elimination diets and a double-blind, placebo controlled food challenge are the main diagnostic procedures (Patriarca et al., 2009). The diagnostic approach to suspected food hypersensitivity reactions begins with the medical history and the clinical examination. Skin prick testing provides a rapid method to screen patients with suspected food allergy. Detection in serum of a specific IgE is the second step after skin prick tests for the diagnosis of food allergy. If these steps indicate potential food allergy, a food challenge may be used to confirm the food allergy. Assuming that specific foods are suspected to be responsible for an allergic disorder, they can be eliminated from the patients diet, with the aim of eliminating the patient's symptoms and confirming the diagnosis.

The development of a food allergy can be divided into two phases: sensitisation and symptom development (Herz, 2008). The sensitisation phase is characterized by the production of an allergen specific IgE antibodies response and their binding to tissue mast cells. Subsequent exposure of the sensitised individual to the same allergen, or to an immunologically cross-reactive protein, cross-linking mast cell-associated IgEs causes degranulation and the release of pre-formed and newly synthesised mediators (like histamines). This provokes the local and/ or systemic inflammation reactions (Dearman and Kimber, 2009). The latter phase results in structural mucosal changes that limit therapeutic options at this disease stage, which is why strategies to prevent the onset and the persistence of an allergic manifestation are needed (Herz, 2008).

At the time of writing, the only reliable treatment of food allergy is strict avoidance of the problematic foods and food ingredients. Food allergy can have a profound impact on quality of life, not only because of the immediate clinical effects related to individual's allergic condition, but also because of the alterations in daily life that have to be made to prevent the occurrence of symptoms and the influence on psychosocial functioning of the individual (Blok et al., 2007; Oude Elberink et al., 2002; Sicherer et al., 2001).

### 1.2 Food allergy management

The most important goal of food allergy management is to prevent the development of the condition because, when an individual has become food allergic, the only treatments are to avoid known allergenic foods and to treat any allergic reaction with 'as needed' medications (Skripak and Sampson, 2008). At the time of writing, desensitisation therapies are only usable for a select number of food allergic consumers. This means that the only option for many food allergic consumers is to completely avoid all foods to which they are allergic (Skripak and Sampson, 2008).

Many people may play a role in food allergen avoidance. The first are food allergic consumers for whom the allergen avoidance is necessary to prevent allergic symptoms. Depending on the specific allergy, and how commonly the food is used as an ingredient to more food products, this has very broad consequences. The alterations to daily life that are made to avoid allergens may also affect the families of food allergic consumers (Bollinger et al., 2006; Oude Elberink, 2006).

Second is the food industry who has a responsibility to produce food that is safe for all consumers. Often foods that may have been in contact with allergens are labelled with may-contain labelling, which is confusing for food allergic consumers (Cornelisse-Vermaat et al., 2008b). Third, health professionals and scientists may facilitate allergen avoidance by improving information about the disease and its management to food allergic consumers. In addition, better diagnostic techniques may lead to a better understanding of what foods cause allergic reactions and therefore may lead to more accurate allergen avoidance (Mills, 2007).

Fourth, regulators provide legislation that addresses the safety of foods, which includes allergenic safety. The food industry has the responsibility to produce foods that are safe for consumers, including food allergic consumers. Improved allergen traceability through the food chain may aid consumers with the allergen avoidance (Mills, 2007). The development of hypoallergenic foods may also improve allergen avoidance.

This thesis focuses on allergy management that relates on the one hand to the introduction of novel foods which may have hypoallergenic properties, or which can

substitute for allergenic foods to facilitate allergen avoidance and therefore may have benefits for food allergic consumers. On the other hand, novel foods may have the potential to induce new allergies. This issue will also be considered.

### 1.3 Novel foods

New foods are continuously being developed and introduced onto the European market. Some of these new foods can be regarded as novel foods. In regulatory terms (European Commission, 2008a) novel foods are defined as foods or food ingredients with no history of widespread and safe consumption. The novelty of a food can be the result of:

(1) genetic modification (GM) of the food itself, or its production using genetically modified organisms. Genetic modification is the change of hereditary material by transferring properties of one organism (e.g. plant, animal) into another organism (Tenbült et al., 2005).

(2) the application of novel processing techniques, such as new types of heat processing, non-thermal preservation methods and the application of new processes catalysed by enzymes,

(3) the food in question having no prior history of consumption in general, or in a specific region or country, such as for “natural” imported foods.

Novel foods may be associated with positive attributes such as improved yield, disease resistance, and prolonged shelf-life. In recent years, many food innovations have been targeted at the promotion of good health (Ronteltap et al., 2007). One potential benefit of novel foods that may appeal to some consumers is that of hypoallergenicity. Food allergic consumers may profit from the availability of hypoallergenic novel foods, as well as consumers who have an increased risk of developing food allergies. The concept of hypoallergenicity refers to the elimination, or removal of the biological activity of allergens. In the case of cow’s milk allergy (CMA) hypoallergenic formulas are defined as those tolerated by ≥90% of infants with documented CMA who are exposed to the tested formula following an elimination diet (Herz, 2008; Lifschitz, 2008). However, it is also important to note that other novel foods with new proteins may have the potential to elicit allergenic sensitisation (Lucas et al., 2004).

Theoretically, there are three scenarios in which a novel protein may be a risk for allergenicity. The first is identity/cross-reactivity with a known allergen, which relates to the introduction of a known allergen, or a cross-reactive allergen into a food crop. An example of the product of a gene derived from an allergenic source is the Brazil nut’s 2S

albumin, an allergenic protein that showed reactivity in Brazil nut allergic consumers after its transfer to an experimental GM soybean (Nordlee, 1996). The second scenario refers to the potential to increase the endogenous allergenicity of the target (commonly allergenic) food due to unintended effects on plant metabolism (that impact on the level of expression of endogenous allergens). The risk associated with the introduction of a novel gene that affects endogenous levels of allergens is more controversial. It could be argued that allergic consumers will be avoiding that food already and therefore are not at increased risk. However, increasing levels of an allergenic protein could increase the number of individuals who will become sensitized to the allergen (de novo sensitisation). This is the third scenario in which a protein may be a risk for allergenicity: the novel protein may be a *de novo* allergen that has not previously been experienced by the human population (Dearman and Kimber, 2009). De novo sensitisation to new allergens is a legitimate concern, given that the introduction into the diet of conventionally produced novel foods, such as that of kiwi fruit in the United Kingdom, has resulted in the appearance, and a steady increase in the number of cases of food allergy to this product (Dearman and Kimber, 2009). In addition to the risks associated with novel proteins, allergenicity of a protein may also be affected when novel processing techniques are applied. Food processing may increase or decrease the allergenicity of a protein (Thomas et al., 2007).

### 1.4 Consumer acceptance

For a novel food to become successful as part of food allergy management, consumer acceptance is an absolute requirement. An example of a novel food that has failed to reach widespread adoption is food that has been irradiated to increase shelf life. Despite the fact that the scientific community recognised food irradiation as an effective and safe process, significant consumer resistance has inhibited the application of the technology (Behrens et al., in press).

Societal responses to emerging technologies may be driven by perceptions of both risk and benefit. Similarly, consumer decsion-making may be driven by perceptions of risk and benefit associated with specific products (Ronteltap et al., 2007). In the case of novel foods developed using emerging technologies, it is relevant to consider both consumer attitudes to the production technology, as well as the novel product itself (Schenk et al., 2008).

Consumer acceptance of novel foods as part of food allergy management strategy is a function of the actual and perceived risks and benefits of the novel foods, the type of allergy and the attitudes of the food allergic consumer, and the information

available about the specific novel food. In the case of food allergy, uncertainty about the extent to which the food is truly hypoallergenic, for food allergic consumers, is highly relevant, in particular in the case of allergens which have the potential to provoke severe reactions.

Most information regarding the acceptance of novel foods concerns focus on genetically modified foods. A few publications refer to the application of GM to produce allergen-free or low-allergen novel foods (Astwood and Fuchs, 1996; Fuchs and Goodman, 1998; Mendieta et al., 1997). Using genetic modification for such a purpose may be perceived as a benefit by food allergic consumers (Moseley, 2001). Research by Miles et al. shows that the intention to purchase genetically modified novel foods with specific benefits was higher than the intention to purchase an unspecified genetically modified novel food (Miles et al., 2006a). However, these authors report that consumers are more likely to purchase low-allergen food produced using conventional methods than food produced using genetic modification. Thus a conventional method of production may be preferred by consumers (Miles et al., 2006a). None-the-less, low-allergen food might represent an attractive benefit for food allergic consumers.

Given evidence of consumer concern that genetic modification may actually cause new food allergies, it may be that even if hypoallergenic food is perceived positively by food allergic consumers, the use of genetic modification in the production of such food would be regarded negatively (Miles et al., 2006a). This can also be explained by the fact that consumers may have different attitudes towards a technology and the resulting innovation.

### 1.5 Aim

The aim of the research presented in this thesis is to investigate whether novel foods can be used as part of an allergy management strategy. For novel foods to be used in food allergy management various factors must be considered. These include (1) the actual hypoallergenicity of novel foods, (2) consumer acceptance of novel foods in general and by food allergic consumers in particular, and (3) the potential impact of novel foods on the quality of life of food allergic consumers. Chapter 2 discusses the issues associated with novel foods and food allergy, such as societal acceptance of such products. The potential issues that arise when applying novel foods as allergy management strategy are identified. Chapter 3 describes the results of a stakeholder consultation, and of focus group discussions with food allergic consumers. The most important food allergy concerns held by both food allergic consumers and stakeholders are identified, together with their opinions regarding the potential impact of novel foods

as a risk management strategy. Chapter 4 describes the results from surveys among food allergic and non-food allergic consumers regarding the acceptance of hypoallergenic novel foods and identifies different consumer groups based on attitudes towards the application of hypoallergenic novel foods as food allergy management. Chapter 5 reviews the international legislation regarding the safety of novel foods to determine whether these regulations protect consumer health sufficiently while allowing consumers to profit from the potential novel food benefits. Effective consumer protection through regulation is an essential part of introducing such foods into the food chain. In the final chapter 6, the results and conclusions from the empirical studies are discussed. This chapter also addresses the limitations of this research and the implication for future research. Figure 1.2 provides an overview of the structure of this thesis.

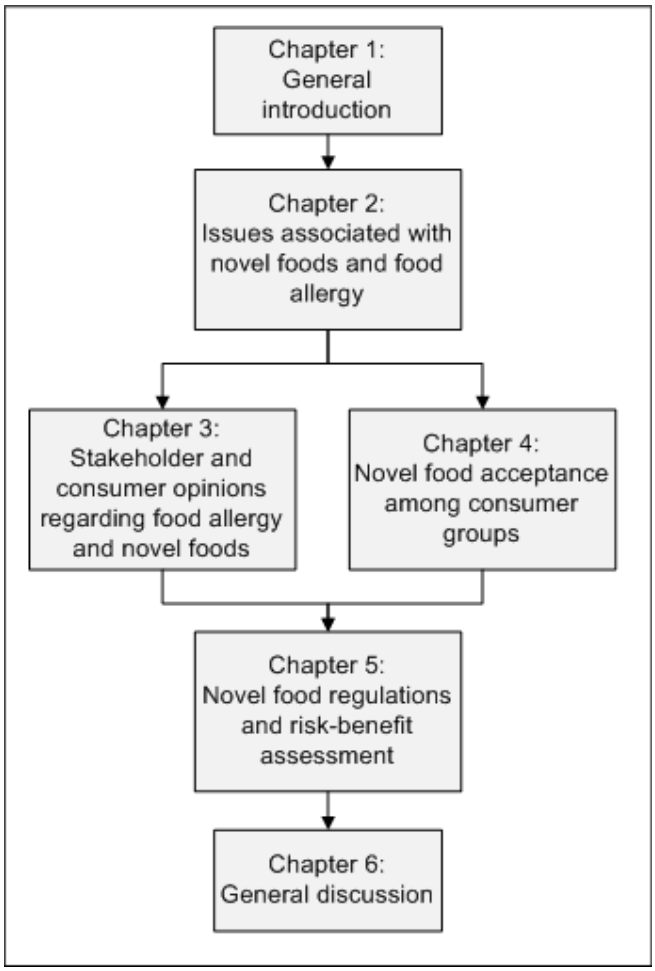


Figure 1.2 Outline of the thesis.

# Chapter 2

## Novel foods and food allergy: the issues

This chapter is published as: Putten, M.C. van, Frewer, L.J., Gilissen, L.J.W.J., Gremmen, B., Peijnenburg, A.A.C.M. & Wichers, H.J. (2006) Novel foods and food allergy: A review of the issues. Trends in Food Science & Technology, 17 (6), 289-299.

**Abstract**

This review identifies and explores the current issues around different types of novel foods and allergy concerns. An important issue relates to the observation that risk estimates associated with novel foods may differ depending on whether more emphasis is placed by the individual on the results of technical risk assessment or on an individual's perceptions of risk associated with different hazards. Consumer perceptions of benefits associated with novel foods also vary. Perceptions of what constitutes both risk and benefit appear to be important determinants of consumer acceptability of particular products. One conclusion that can be made is that novel foods have the potential to contribute to food allergy management, but that consumer acceptance is likely to differ according to the preferences of individual consumers. It is concluded that some novel foods may result in improvements on the quality of life of food allergic patients, whereas others may result in the development of further socio-economic problems.

## 2.1 Introduction

This review aims to identify and explore issues around novel foods and food allergies. A *food allergy* is defined as an aberrant fast immunological reaction to normally harmless food components, usually proteins (Sampson, 1999a). Food allergy is distinguished from *food intolerance*, which is a non-immune-mediated reaction. In contrast with food allergy, symptoms of food intolerance can take several days to manifest themselves. *Novel foods* are defined as foods or food ingredients that have no history of safe use in the European Union (EU). The absence of a history of safe use can be the result of: (1) genetic modification of the food or production of the food using genetically modified organisms, (2) novel processing techniques, or (3) the food being new to the European Union. That is, although the food has a history of use in other parts of the world, this is not the case in Europe. The latter category is in the context of this chapter referred to as natural novel foods.

There is some evidence that food allergy prevalence is increasing in some parts of the world, although this is not definitively proven (Helm and Burks, 2000). One aspect of food allergy that needs further consideration is that of novel foods. The introduction of novel proteins into the food chain and the human diet may result in new cases of food allergy. In contrast, the elimination of allergenic proteins may lead to reduced risk of allergy. In both cases, consumer and other stakeholder attitudes towards the application of novel technologies to food production complicate the issue of commercialisation of novel foods. For the purpose of this chapter we will consider food allergy and novel foods in the context of the European Union. However, the issues discussed are generic and have international applicability.

Various organisations and individuals have an interest in the issue of food allergy. Examples of stakeholder groups are food allergic individuals and their families, health professionals, the food industry, policy makers, public health authorities, non-governmental organisations (NGOs), patient organisations, scientists and finally the general public, who may have to deal with the issues associated with food allergy on an occasional basis.

This review chapter will discuss the different risks and benefits associated with novel foods within the context of technical risk assessment, as well as public risk perceptions regarding the acceptability of different kinds of novel foods. We will then discuss food allergy prevalence, which may be on the increase, although the literature is varying regarding this issue. Quality of life may be negatively affected by food allergy (Sicherer et al., 2001) and also needs to be addressed. In addition, different strategies for allergy management and the role novel foods can play in the development and

enactment of allergy management will be discussed. Finally, future research needs will be identified.

## 2.2 Novel Foods

Novel foods may be introduced into the food chain in order to attain some associated potential societal or environmental benefits, (Rowland, 2002) but may also be associated with some (perceived) risks (Shewry et al., 2000). We provide an overview of the risks and benefits associated with novel foods, as both these factors are likely to influence the acceptance of novel foods by consumers.

### 2.2.1 Risks and benefits

Genetically modified foods

There is an extensive literature regarding consumer attitudes to the introduction of genetically modified foods, particularly in Europe (Frewer et al., 2004). Various factors determine consumer acceptance of genetically modified foods, including those relating to perceptions of involuntariness of exposure regarding individual consumption, inability to trace genetically modified foods and ingredients in the food chain, and perceived unnaturalness of food products and production methods. In the area of health, many consumer concerns about genetically modified foods are related to the uncertainty of the (potentially long term) effects on consumer health in general (Frewer and Salter, 2003; Miles and Frewer, 2001) including increased allergenicity associated with the introduction of novel proteins into the human food chain (Shewry et al., 2000). An example of this is the 2S albumin in the Brazil nut which was used in transgenic soy bean, to which some consumers are allergic.

Although the process of genetic modification may introduce new allergenic proteins into foods, it can also be used to remove established allergens (Kuiper et al., 2002; Shewry et al., 2000). At the present time, it is unknown whether food allergic consumers would be willing to buy and use these hypoallergenic foods, or whether allergic consumer acceptance would be contingent on the severity of the allergic reaction experienced (Schenk et al., 2008).

Benefits associated with genetically modified novel foods include improved yield, enhanced plant disease resistance, improved taste and other quality parameters, and improved growth in adverse conditions such as drought and low temperatures (Rowland, 2002). Many of these benefits are similar to those that have been achieved in conventional breeding programs. However, whereas some traditional breeding techniques aim at changing as many genes as possible in the plant genotype in order to

produce the desired changes, genetic modification permits the expression of the target gene(s) alone.

Consumer's perceptions of the risks and benefits of genetically modified foods influence acceptance or rejection of specific products. Miles et al. (2001) have demonstrated that the extent of the accrual of benefits, and to whom these benefits accrue, (for example, to industry or consumers) appears to be an important factor in consumer acceptance (Miles and Frewer, 2001). To date, most of the advantages conferred by genetic modification in the agrifood sector are linked to improvements in agronomic traits, which have no direct benefit for consumers. Thus, if we assume that consumer acceptance of genetically modified foods is underpinned by consumer recognition that there are direct benefits to consumers, it is unlikely that improvement in agronomic traits alone will result in consumer approval of novel products (Frewer et al., 2003b; Miles and Frewer, 2001; Saba et al., 1998).

Genetic modification of crops may result in novel foods with improved quality characteristics, improved nutritional and health attributes, resistance to spoilage and even reduced levels of allergens, which have a direct benefit for consumers (Kuiper et al., 2002; Taylor and Hefle, 2001). Research by Saba et al. (1998) indicates that some consumers would be willing to buy genetically modified foods with consumer oriented benefits (Saba et al., 1998). However, at the present time, more research is needed to clarify whether consumers would be willing to buy genetically modified foods with benefits in terms of reduced allergenicity.

Foods produced using other novel processing techniques

Examples of processing techniques that are at the time of writing, considered "novel" are thermal processing, high-pressure processing, ultra filtration and γ-irradiation. All of these techniques have been introduced in order to improve food safety and quality. Application of these techniques may reduce *or* increase allergenicity (Davis et al., 2001). For example, the impact of thermal processing on the presence of food allergens depends on which specific allergens are present in the food. The major apple allergen, Mal d 1, is a protein that degenerates easily following thermal processing. This denaturation changes the structure of the protein, which makes it impossible to be recognised by immunoglobulin-E (IgE). As a consequence, the consumer does not suffer from an allergic reaction to the protein. In contrast, some fish allergens do not produce an adverse reaction when the product is fresh, but produce an allergic response after these are cooked (Davis et al., 2001; Wigotzki, 2001). Further analysis is required to determine systematically which allergens are activated and which ones are eliminated during various methods of novel processing. The benefits of novel processing techniques

include increasing the shelf life of products without negatively altering structure and taste.

Natural novel foods

The major risk associated with natural novel foods is that they contain proteins that may provoke allergic reactions within populations where they have been newly introduced into the diet. This increased risk is the result of globalisation and increased allergen distribution through the world. Related to this is the risk that the new proteins are cross-related to known allergens, or those which are already extant in a particular food chain. The major benefit of natural novel foods is the increased diversity of food from which consumers can choose and possibly as a consequence, the increase of healthy compounds in the diet (Bäckström et al., 2003).

### 2.2.2 Risk Conflict

Different individuals appear to evaluate the risks and benefits of novel foods in different ways, and this also varies across different applications. Very broadly, it appears that there are differences between the way that experts and non-experts evaluate risks, an observation established over many different types of hazard (Slovic, 1999). In the present discussion, we refer to this difference as risk conflict.

Technical risk assessments are frequently the basis of risk management practices within the risk analysis framework. Technical risk assessments are often used by experts and regulators to determine acceptable safety levels (Taylor and Hefle, 2001), although consumer decision-making is, in part, based on broader, societally relevant factors of concern (Frewer et al., 2004). The latter will be discussed in the next section. Assessment of potential allergenicity is, of course, only one component of the risk assessment of novel foods (Kuiper et al., 2002; Rowland, 2002). Microbiological and toxicological risks are also important, although they are not relevant to the topic of allergenicity.

Consumer risk perceptions

Risk perceptions are a specific form of attitude towards a particular object, such as a potential food hazard (Frewer et al., 2004). These include factors such as the extent to which an individual perceives the risk of a hazard to be uncertain, dreaded, potentially catastrophic, uncontrollable, equitably distributed and presenting risks to future generations and influence people's acceptance of a particular hazard (Slovic, 1999). This broad concept of risk implies that psychological responses to a particular hazard may not

directly relate to technical risk estimates resulting from a formal risk assessment procedure. In contrast, experts tend to see risk as synonymous with probability of harm, or expected mortality, consistent with the way in which risk tends to be characterised in risk assessment. Therefore, technical risk estimates, traditionally provided by experts, influence people's behaviours in a different way than risk perception (Frewer et al., 2004). As a result, many conflicts over the risk of foods may result from different stakeholders having different perspectives (Slovic, 1999). For example, in the case of Starlink maize, most experts estimated the chance of Starlink provoking an allergic reaction in human consumers to be very small. Despite these reassurances from the expert community, the discovery of Starlink maize in tacos destined for human consumption was viewed negatively by the consumer, and consequently resulted in the recall of almost 300 maize products (Gremmen et al., 2004).

People's responses to risk are psychological, such that people's perceptions about a particular hazard influence their responses to it (Frewer et al., 2004). The social context of risk also plays an important role in how people represent risk (Joffe, 2003). Social representation theory can provide a useful framework for examining risk perceptions of novel foods and the way science enters the domain of everyday thinking (Bäckström et al., 2003). Social representations can be defined as systems of relevant values, ideas and practices (Moscovici, 2000), and can be used for research focussed on the social construction of social knowledge (Flick et al., 2002). Bäckström et al. (2003) have demonstrated using social representation theory that the risk perceptions associated with novel foods are multidimensional (Bäckström et al., 2003). In other words, people make sense of unfamiliar novel foods using various dichotomies, such as trust/distrust, safe/unsafe, natural/artificial, pleasure/ necessity and past/present. The artificial and unnatural nature of foods produced using genetic modification has been identified as an important dimension for consumer negativity towards these products (Bäckström et al., 2003). Trust in science and regulators, or a lack of it has been identified as a potentially important determinant of consumer acceptance of novel foods (Frewer et al., 2003a).

Genetically modified novel foods

Governmental regulatory agencies in most developed countries require a mandatory safety assessment and consultation with governmental regulators before commercial sale of genetically modified foods is permitted (Taylor and Hefle, 2001). However, the assessment process applied to determine the allergenic potential of genetically modified foods presents major problems, since there are no reliable tests for predicting clinical allergenicity. As a consequence, assessment of allergenic potential

has often focused on determining whether the novel product is *substantially equivalent* to the traditional counterpart (Taylor and Hefle, 2001). The safety of traditional foods and ingredients is usually accepted on the basis of their history of safe use. As a consequence, there is general consensus that, where possible, safety assessment should use traditional foods and ingredients as reference points, and that assessment processes should focus on the differences between these traditional foods, and the novel foods and ingredients under assessment (Howlett et al., 2003). If a novel food is determined to be substantially equivalent, then it is judged to be as safe as its traditional counterpart. If the novel food is not substantially equivalent it needs to be subject to a broader analysis on a case-by-case basis, with the safety assessment focussing on established differences between the novel food and its conventional counterpart (Taylor and Hefle, 2001). An established decision-tree approach for predicting the potential allergenicity of novel proteins is that of the Codex Alimentarius and the Food and Agriculture Organisation / World Health Organisation consultation group. This decision tree approach, which assumes that the amino acid sequence is known, is discussed frequently in the existing literature (for example, see Taylor et al., 2001).

Applying this approach provides reasonable assurance that the newly introduced protein has limited capability to develop into an allergen (Taylor and Hefle, 2001). However, it is important to realise that *absolute safety* is not an achievable standard, since all technologies hold known and unknown risks (Garza and Stover, 2003). This uncertainty is one of the risks frequently mentioned by consumers (Miles and Frewer, 2001).

When during this risk assessment process no particular concern is indicated for any specific population group (not only known food allergic individuals), the occurrence of non-immunologically based reactions may still become apparent post-launch. This indicates the need for post-launch monitoring (Howlett et al., 2003). It should be noted that application of the substantial equivalence approach does not satisfy consumer concerns associated with the application of genetic modification more generally. For example, a consumer concerned about the potentially negative impact of genetically modified crops on the environment, independent of the absence or otherwise of novel proteins in foods to be consumed, may not be reassured by claims of substantial equivalence of novel foods (Frewer et al., 2004).

Foods produced using other novel techniques and ethnic novel foods

It should be noted that expert risk assessment focuses on the novel protein as unit of analysis, rather than the complete food. This is because a few genes are introduced into a particular genome. As a consequence, it remains exactly the same,

except for these genes, so it is only necessary to focus on the new protein which results from the inclusion of additional genes (Howlett et al., 2003). However, for foods that are produced with the use of novel processing techniques, and for natural novel foods, it is not sufficient to assess whether a single protein has been produced. In the case of various processing techniques it is not effective to assess the amino acid sequence, because in most cases the amino acid sequence does not change. Instead, it is the protein structure that changes and that reveals or hides an epitope, which is the binding site on a protein for IgE.

In the case of natural novel foods it is not possible to focus on a single protein because the product may not have been introduced into a particular food chain before and, in the case of foods introduced into the European market, possess a genome that has not been described previously. It is therefore not possible to examine the amino acid sequence of specific foods, and the decision tree approach cannot be applied to natural novel foods. However, in most of these cases, it is possible to identify an established food that is similar, either in terms of plant function, or because it has a botanical relationship to the natural novel food. It is also possible to screen for known allergenic proteins in the natural novel food. These proteins can be compared to known allergenic proteins. This means that it is possible to use the substantial equivalence principle, and as a result the natural novel food is considered safe if the comparable counterpart has a history of safety (Howlett et al., 2003; Kuiper et al., 2002).

Of course, it is arguable that experts also apply factors other than those grounded in rationality (Jensen and Sandøe, 2002). Thus it is important to acknowledge that experts apply values to risk assessment, and lay people are capable of reasoning. However, experts tend to utilise arguments originating in technical risk assessment to a greater extent than do the public in proposing different arguments about risks of novel foods (Gremmen et al., 2004).

### 2.2.3 Novel food acceptance

In the area of (food) technology innovation, people may tolerate some level of risk associated with (for example) production processes if they also perceive direct benefit to themselves as consumers, rather than to other groups in society, such as producers or the food industry (Frewer, 2003). Scientists and industrialists have, in the past, assumed that consumers will accept novel products with a specific consumer benefit. However, just as the public, to some extent, defines risk in a different way to experts (Kleef et al., 2006), it is possible that the public also defines benefits differently. In addition, what is perceived to be a benefit associated with a novel food differs between different countries

and cultures, and between different individuals at different times and within different contexts (Frewer et al., 2004). Genetically modified foods with reduced or absent allergenicity may be perceived as highly beneficial by food allergic consumers and thus acceptable. For non-allergic consumers, the perceived risks may outweigh the benefits. It might be concluded that, as long as risk is not so large as to be completely intolerable, an individual's acceptance will be driven by perceptions of personal benefit (Frewer, 2003). However, individual differences in attitude, in part shaped by personal needs and requirements also need to be taken into account. We can explain the relative acceptability of natural novel foods when compared to genetically modified foods. The introduction of novel foods from different cultures, may be accepted by a particular group of consumers more easily because they have already been "tested" by other people (Bäckström et al., 2003), or because they are considered to be natural in origin, and thus tolerable.

There is thus some theoretical evidence regarding the factors which may influence consumer acceptance of novel foods, at least in Europe. It remains unclear, however, whether consumers will accept novel foods *in practice*. Technical risk assessment processes currently used by risk assessors and regulators is only of partial utility in developing a risk communication strategy, as it does not address some important consumer concerns.

### 2.3 Food allergy and society

It is said that the prevalence of food allergy is increasing (Helm and Burks, 2000). In order to assess the extent of the food allergy problem it is important to understand the reported prevalence of food allergies.

#### 2.3.1 Food allergy prevalence

Although the increasing prevalence of food allergy is *frequently mentioned* in the food allergy literature, information regarding *formal* assessment of the *epidemiology of food allergy* is less often presented (Altman and Chiaramonte, 1996; Crevel, 2002; Fraser et al., 2000; Helm and Burks, 2000; Kagan, 2003; Kimber and Dearman, 2002; Oehlschlager et al., 2001; Thompson and Chandra, 2002; Zeiger, 2003). Only a few articles have reported primary data on food allergy prevalence (Eigenmann et al., 1998; Sicherer et al., 1999; Sicherer et al., 2003; Woods et al., 2001). At the present time, it is not understood whether the introduction of novel foods will contribute to an increase in food allergies, or if genetically modified novel foods with reduced allergenicity will significantly reduce food allergy prevalence. This requires close monitoring in the future.

Table 2.1 gives an overview of food allergy prevalence for both children and adults reported in different literature sources. One distinction that is made in this table is between the prevalence of “true” food allergy and “perceived” food allergy. True food allergy prevalence refers to the percentage of patients in a population with a formal diagnosis of food allergy. Perceived food allergy prevalence refers to the people’s belief that they personally exhibit the symptoms of a food allergy, independent of whether a health professional would diagnose them as food allergic. This means that the self-reported data leading to population level estimates of prevalence of perceived food allergy may include both food allergy and food intolerance and maybe even other adverse reactions to food. This explains why the public’s perception of food allergy prevalence may be much higher than is supported by the actual prevalence data. The data summarised in Table 1 show that there is no agreement within the existing literature regarding the prevalence of food allergy. One of the reasons for this lack of agreement is that it is difficult to diagnose food allergy. The Double-Blind-Placebo-Controlled Food Challenge (DBPCFC) is both expensive and time consuming for patient and doctor. Other diagnosis methods are Radioallergosorbent tests (RAST) in which the amount of specific IgE is tested, and skin prick tests (SPT) where glycerinated diluted food extracts are applied to the skin by prick technique (Sampson, 1999b). It is important to note that there are two phases of food allergy: the primary contact with an allergen and the later repetitive contact with an allergen, which results in symptoms (Mills et al., 2003). Some individuals become sensitised, but never develop the symptoms. These individuals will get positive results from RAST assays and SPT, but a DBPCFC will give negative results. Diagnosis is therefore highly dependent on the diagnosis method used, which clearly contributes to ambiguities in food allergy prevalence rates. Other diagnosis methods available are questionnaires and self-report data. These are not reliable methods of food allergy diagnosis because food allergy symptoms are often similar to those associated with other adverse reactions to food, (for example nausea), which results in a higher reported food allergy prevalence than actually is the case. Another problem in developing accurate prevalence estimates is that only a few studies analyse food allergy prevalence across *complete* populations, as opposed to population segments. This is illustrated by the study of Eigenmann et al. (1998) who report a food allergy prevalence of 37% in a population of children suffering from atopic dermatitis (Eigenmann et al., 1998). Although the prevalence in this population could be accurate, it makes comparison of prevalence rates with other studies and other populations difficult. In addition, there is a lack of uniform definitions of various adverse reactions to food,

Table 2.1 Food allergy prevalence 1

| Year[1] | Prevalence | Diagnosis[2] | Food[3] | C/A[4] | Population[5] | Country[6] | Source |
|---|---|---|---|---|---|---|---|
| 1980-1984 | 28% | Parentally reported FA | No specific foods | C | 480 children followed prospectively from birth to their third birthdays | USA | (Bock, 1987) |
| | 8% | DBPCFC | | | | | |
| Before1988 | 5.3% | Parentally reported FA | No specific foods | C | Infants 0-6 months | The Netherlands | (Douwes, Weert-Waltman van, Folkertsma, Fagel and Verboom, 1988) |
| | 1.7% | Open food challenge | | | | | |
| 1989-1992 | 12.4% | Self reported Food allergy/ Food intolerance | No specific foods | A | Healthy Dutch adults 1483 individuals | The Netherlands | (Niestijl Jansen, Kardinaal, Huijbers, Vlieg-Boerstra, Martens and Oc khuizen, 1994) |
| | 2.4%[7] | DBPCFC | | | | | |
| 1991-1994 | 12% | Self reported FA/FI | No specific foods | A | Cross sectional sample of 17280 adults aged 20-44 years | 14 European countries and USA | (Woods, et al., 2001) |
| Before 1994 | 1.4-1.8[8] | Self reported FI | No specific foods | A+C | 15000 households (7500 cross sectional, 7500 randomly selected nationwide | UK | (Young, Stoneham, Petruckevitch, Barton and Rona, 1994) |
| 1997 | 0.6% | Self reported allergy | Peanut or tree nut allergy | C | 4374 households nationwide sample Children under 18 years | USA | (Sicherer, et al., 1999) |
| | 1.6% | | | A | 4374 households nationwide sample | | |
| Before 1998 | 37% | IgE (6 foods) | Milk, egg, peanut, soy, wheat, fish | C | 63 patients with atopic dermatitis between 0.4 to 19.4 years | USA | (Eigenmann, et al., 1998) |
| 2002 | 1.2% | Self reported | Peanut or tree nut allergy | C | 4855 households nationwide sample | USA | (Sicherer, et al., 2003) |
| | 1.3% | | | A | 4855 households nationwide sample | | |
| 2002 | 0.6% | Self reported | Sea food allergy | C | 5529 households nationwide sample | USA | (Sicherer, Muñoz-Furlong and Sampson, 2004) |
| | 2.8% | | | A | 5529 households nationwide sample | | |

[1] The year in which the study was conducted.

[2] The diagnosis column refers to the method that was used to diagnose the participants of the study.

[3] In this column is indicated whether the reported prevalence rate applies to a specific type of food.

[4] C and A indicate whether the study was focused on children, adults or on both.

[5] Information about the sample and population the sample was drawn from.

[6] County in which the study has been done.

[7] Estimated, based on Double-blind Placebo-controlled Food Challenge and on the assumption that FA/FI is equal among participant, non-participants and drop-outs.

[8] 1.4% with stringent criteria and 1.8% with less-stringent criteria.

resulting in problematic interpretation of research findings. The effect of this can be seen in the third column of Table 2.1 where the definitions of food allergy used in patient diagnosis vary across research studies. There is, however general agreement that the prevalence of food allergy in children is higher than in adults (Altman and Chiaramonte, 1996; Bock, 1987; Chandra, 1997; Crevel, 2002; Kimber and Dearman, 2002; Sampson,1999a). The greater prevalence in children can be explained by an increased predisposition of children to develop food allergy, and by the tendency for children to develop immunologic tolerance as they get older.

However, due to the incomparability of the data presented in table 1 it is not possible to conclude that food allergy prevalence has increased. The only studies that show a small increase in peanut and tree nut allergy prevalence are those of Sicherer et al. who found a slight increase in prevalence in children of over five years of age (Sicherer et al., 1999; Sicherer et al., 2003). However, there is some indirect evidence that indicates that food allergy prevalence is increasing. The first indication for this increase is cross sensitisation, which means that food allergy often occurs in combination with other allergies. It has been established that the prevalence of other allergic diseases such as pulmonary or occupational allergies is increasing, which suggests that the prevalence of food allergy might be increasing in line with this general trend (Jansen and Brussaard, 2001). Another indication of increased prevalence is provided by the observation that peanut allergy is becoming more common in younger generations, but not in older ones (Hourihane et al., 1996). Since peanut allergy is rarely outgrown, it can be expected that peanut allergic children will continue to suffer from peanut allergy as they get older. The third indication is the fact that, as a consequence of the increase of global trade, the variety of food consumed at the present time is higher than in the past. As a result, people will be increasingly exposed to a wider diversity of food antigens, which may result in increased food allergy (Fraser et al., 2000; Jansen and Brussaard, 2001).

### 2.3.2 Socio-economic impact

Food allergies can have a significant impact on the quality of life and economic functioning of people who suffer from them, as well as wider implications for society more generally. The economic impact of food allergy is composed of both direct and indirect costs. Direct costs include both medical and non-medical expenses associated with the disease, such as prevention and treatment costs and transportation costs associated with healthcare provision (Gergen, 2001). Indirect costs are linked to factors such as work and productivity. The introduction of novel foods with reduced allergenicity may be

readily accepted if these foods have a positive effect on quality of life and economic functioning. However, it is unlikely that improvements in socio-economic functioning of food allergic patients in isolation of other societal benefits will facilitate global marketing of foods previously confined to specific ethnic groups or geographical locations, because such benefits only apply to a limited number of people. The economic impact of food allergy is difficult to estimate because of a lack of knowledge about the population-level prevalence. In addition, a cost for one stakeholder group may represent a benefit to another stakeholder group. In the case of allergy, for example, medication will result in costs for patients or insurance companies, but generate profits for the pharmaceutical companies. Patients will, of course, also benefit from alleviation of symptoms (Mugford, 2004). In the European White Paper on Allergy (1997) the socio-economic costs of allergy have been estimated. The total costs of the major allergic diseases (including allergic rhinitis, allergic asthma, atopic dermatitis, contact dermatitis and urticaria) are estimated at 10 billion ECU for direct costs and 19 billion ECU for indirect costs. Food allergy is not mentioned as one of the major allergic diseases in this report, perhaps because of the paucity of information available to permit cost estimation regarding direct and indirect costs (Aas et al., 1997).

Generally speaking, the costs of food allergy are conceptualised in different ways by different stakeholder groups within society. If the economic costs are assessed by risk regulators and public health authorities, one might expect that both direct and indirect costs are considered important, and thus should be taken into account when implementing a strategy regarding the commercialisation of novel foods, whether from the perspective of allergy reduction, or reducing any potential for increased prevalence of food allergy. From the food manufacturers and retailers point of view, the direct costs tend to carry greater weight, because they tend to influence the cost of business activities. From an industrial perspective, indirect costs are of less importance as quality of life is not a direct issue. The liability of food manufacturers regarding hidden allergens in products is an increasingly relevant issue, as liability claims can have an impact on direct costs of food manufacturers if labelling is inaccurate (Crevel, 2002).

The indirect costs of food allergy have a much greater impact on individuals and families, because these costs reflect the functioning and quality of life of the individual and the family where a family member suffers from a food allergy (Gergen, 2001). The social impact of food allergy primarily relates to potentially negative effects on quality of life (QoL). Food allergy can have a profound impact on quality of life, not only because of the immediate clinical effects related to individual's allergic condition, but also because of the alterations in daily life which are needed in order to prevent the occurrence of food allergy symptoms and the influence on psychosocial functioning of the individual

(Sicherer et al., 2001). Reactions that can occur when a food allergic individual is exposed to allergens range from abdominal pain, vomiting and/ or diarrhoea to cardiovascular symptoms, including hypotension, vascular collapse and cardiac dysrhythmias. Exposure to a food allergen can even result in anaphylaxis, which may be severe enough to be life-threatening (Sampson, 1999a). Thus food allergy may result in restriction of social activities (for example, eating outside the home, more problematic shopping expeditions) and anxiety (Knibb et al., 2000). The only reliable therapy used to treat food allergy at the present time is restriction or complete elimination of the responsible food allergen and emergency management of reactions in case a food allergen is accidentally ingested. Needless to say, this has a negative impact on the quality of life of both the food allergic individual and their families (James, 2001), as well as an emotional impact (Meltzer, 2001), and psychological distress (Knibb et al., 1999), and restrictions on leisure activities and other lifestyle factors (Knibb et al., 2000). Whilst labelling is informative (Crevel, 2002), and essential for consumers with a diagnosed food allergy (Mills et al., 2004), the introduction of novel allergens may result in allergic responses independent of a labelling policy, as individuals will not know to which foods and ingredients they will experience negative reactions.

## 2.4 Management of food allergies

### 2.4.1 Prevention

An important step of food allergy management is prevention. Zeiger (2003) identifies three phases of prevention, *primary*, *secondary* and *tertiary.* Primary prevention essentially means blocking of immunologic sensitisation and thus reducing the prevalence. Secondary prevention is interpreted as suppression of disease symptoms after immunologic sensitisation has occurred. Tertiary prevention represents the stage in which symptoms are treated and worsening of the patients situation is prevented (Zeiger, 2003).

<u>Primary prevention</u>

Primary prevention appears to be beneficial only for infants with an atopic family history (Zeiger, 2003). A critical time in early infancy can be identified in which the genetically programmed atopic infants are at higher risk to become sensitised to ingested and/or encountered food allergens. Prenatal exposure may also be problematic in terms of sensitisation. Some novel foods can help in primary prevention as they do not expose the child to potential allergens. However, it cannot be assumed that all food allergens are already identified. This means that it may not be possible to avoid the yet unidentified food allergens. This could be the case with natural novel foods, since their

amino acid sequence is, in most cases, unknown. In addition, it is difficult to identify in advance which proteins in novel foods could cross-react with known allergens. Predictive testing of food to identify allergens is a method of primary prevention, because it enables risks to be identified, which is the basis for control, but this procedure cannot identify the risk of cross-reactions (Smith, 1997). Thus primary prevention of food allergy should focus not only on food allergens, but also on the avoidance of allergens that are not directly causing food allergy, but might do so due to cross sensitisation, as is the case with birch allergens.

Secondary prevention

Once sensitisation has occurred, avoidance of the food allergens is the only proven strategy to prevent the occurrence of symptoms. Strict elimination diets may lead to malnutrition, especially if they include a large number of foods and/or are used for extended periods of time (Sampson, 1999b). Elimination of a single food can be difficult, especially when the food is used in many other food products, such as milk. Labelling is an important part of secondary prevention because it enables individuals to avoid foods to which they are already hyper-sensitised (Smith, 1997). A prerequisite for this is that the information on the label is readily understood by the consumer (Crevel, 2002).

It should be noted that there is a difference between treatment of a disease and life-long avoidance (Kilshaw, 1981). In case of food allergies, the impact of avoidance on the daily lives of food allergic consumers and their families forms a major part of the socio-economic problems associated with food allergy. Avoidance is therefore not a real solution for the food allergy problem, although it currently is the most important part of food allergy management. Novel foods can help with secondary prevention because their potential for inducing allergic responses may be reduced.

Tertiary prevention

Given the difficulty of avoiding food allergens, it must be assumed that patients may experience accidental ingestion of problematic foods. Contamination with an unrelated food during the manufacturing process or misrepresentation of a food item on a label are common causes of accidental exposure to known allergens (Thompson and Chandra, 2002). Medications, such as anti-histamines, have been used in an attempt to modify symptoms of food-induced allergic disorders, but overall they have minimal efficacy. Oral corticosteroids are generally effective in treating chronic IgE-mediated disorders, but side effects are generally unacceptable to patients (Sampson, 1999b). In case of anaphylaxis, injection of epinephrine is the primary treatment, even in the early stages before the onset of life-threatening symptoms, as treatment failure is more likely if epinephrine is

delayed (Thompson and Chandra, 2002). Children with symptomatic food allergy often lose their allergy over time. Exceptions tend to occur in most cases of peanut, tree nut, and seafood allergy (Sampson, 1999b). Consequently, food challenges should be repeated at set intervals to determine whether the dietary restrictions are still necessary (Bruijnzeel-Koomen et al., 1995).

Tertiary prevention involves medication of symptoms and therefore it is unlikely that novel foods can play a role in tertiary prevention.

Conclusion

It is obvious that primary prevention, the prevention of sensitisation, is the best strategy to decrease the food allergy prevalence, because this type of prevention reduces the socio-economic impact on the daily lives of food allergic consumers and their families. Secondary prevention does not really prevent allergic disease, but only prevents the occurrence of symptoms. In an ideal situation secondary prevention is not necessary, because primary prevention would have proven to be successful. Given that tertiary prevention is nothing more than treatment of the symptoms, it still represents an important part of food allergy management, as these symptoms can be severe, or even fatal.

### 2.4.2 Novel foods applied to food allergy management

The incidence of severe (and potentially fatal) food-induced allergic reactions indicates that current management strategies (allergen avoidance and early use of epinephrine) are not adequate for dealing with food allergies (Leung and Bock, 2003), suggesting that additional management strategies are needed. Novel foods may facilitate food allergy management. One approach under investigation involves the mutation of IgE binding epitopes on major peanut proteins. The mutated recombinant protein may desensitise patients with peanut allergy in a manner similar to standard immunotherapy without the risk of inducing anaphylactic symptoms (Sampson, 1999b). Another approach under investigation involves the development of hypo-allergenic foods. In these foods, most allergens have been removed chemically, enzymatically or by formulating the food product from different ingredients. For example, rice has been genetically modified to suppress the expression of a gene encoding for a certain allergen (Laiho et al., 2002). However, it is unlikely that *all* consumers will accept the introduction of genetically modified rice into the food chain, particularly those not suffering from food allergy. However, allergic consumers may be enthusiastic about these novel foods, resulting in the development of niche markets for hypoallergenic food products.

Differences in the neonatal gut micro biota may precede the development of atopy. The modification of the gut micro biota by means of novel foods induces beneficial effects that may reduce the risk of allergic disease (Nowak-Wegrzyn, 2003). Allergic disease could be prevented through nutritional management capable of preventing or depressing allergic inflammation based on the administration of novel foods containing strains of beneficial microbes (Laiho et al., 2002). However, again the issue of product acceptability based on consumer response may need to be addressed.

### 2.5 Conclusions

In this review we have identified various issues surrounding novel foods and food allergy. An important issue is that there are both risks and benefits associated with novel foods. Consumer acceptance of novel foods is contingent on both technical risk estimates, and consumer perceptions of both risk and benefit. Furthermore, consumers are not homogenous, and what is perceived as a desirable benefit by one consumer may be regarded as irrelevant by another. In the case of novel foods, genetic modification directed towards reducing allergenicity may be viewed positively by allergic consumers, but is unlikely to meet with general consumer approval. This suggests that such products should be marketed specifically to consumers who want to buy them, under conditions of fully informed consumer choice.

Consumers perceive ethnic novel foods are less risky than genetically modified foods (Bäckström et al., 2003). However, the example of kiwi fruit proves that natural novel foods cannot be considered safe from an allergy point of view without proper safety analysis (Bublin et al., 2004; Lucas et al., 2004).

It can be concluded that novel foods, despite some risks, have the potential to contribute to food allergy management. They can contribute particularly to primary and secondary prevention by avoidance of the concerning allergens. For tertiary prevention, novel foods are less helpful. However, novel foods can also potentially increase the prevalence of food allergy through introduction of novel or unlabelled allergens into the human food chain, and this needs to be carefully assessed. It remains unclear what are the allergy risks for novel foods that are not genetically modified, perhaps indicating the need for implementation of a decision tree similar to that applied to genetically modified novel foods.

**Acknowledgements**

This literature review has been done as part of a PhD project funded by the Allergy Consortium Wageningen, The Netherlands.

# Chapter 3

# Stakeholder and consumer views regarding novel hypoallergenic foods

This chapter is accepted for publication as: Putten, M.C. van, Gilissen, L.J.W.J., Gremmen, B., Peijnenburg, A.A.C.M., Wichers, H.J. & Frewer, L.J. (in press) Stakeholder and consumer views regarding novel hypoallergenic foods. British Food Journal

**Abstract**

The development and introduction of novel hypoallergenic foods represents a potential approach to reducing the negative health impacts of food allergy. The aim of this research is to assess whether novel hypoallergenic foods will be accepted by food chain actors and consumers. Stakeholder opinions (collated using semi-structured interviews, N=16) regarding the acceptability of novel hypoallergenic foods were assessed. Three focus groups (one comprising anaphylactic food allergic consumers, and two comprising consumers with less severe food allergies) were applied to understand the opinions of food allergic consumers. Food allergic consumers expressed a preference for a "cure" for food allergy. However, they acknowledged that hypoallergenic foods had the potential to improve the quality of lives of food allergy suffers through increasing dietary variation, and reducing restrictions on product selection. Stakeholders supported the introduction of novel foods (although this support was not universal), assuming the products were acceptable to food allergic consumers, consumers in general, and regulators. The results cannot be extrapolated to the general population because of small sample sizes. However, the results are indicative of potentially important factors determining societal acceptance of novel hypoallergenic foods in the future. The issue of whether such novel foods would be acceptable to non-food allergic consumers was not addressed. The chapter is likely to be useful for the potential developers of hypoallergenic foods allergen food products (food industry and scientists) and policy makers regarding the commercialisation of novel hypoallergenic foods and their regulation.

### 3.1 Introduction

Food allergy represents an increasing concern to society. Food allergy is defined as an inappropriate immunological reaction to normally harmless food components and affects 5-8% of children and 1-2% of adults (Buttriss and Schenker, 2002; Rona et al., 2007; Sicherer et al., 2001). Food allergies potentially have a negative impact on the quality of life (Blok et al., 2007; Sicherer et al., 2001) and economic functioning of food allergic patients (Cornelisse-Vermaat et al., 2008b; Fernandes-Rivas and Miles, 2004; Fox et al., in press) and may also result in substantial costs for society overall in terms of health care costs and absenteeism (Blok et al., 2007; Miles et al., 2005). The only effective treatment for food allergy available at the time of writing is for food allergy sufferers to avoid problematic foods (Ortolani and Pastorello, 2006), which may negatively influence the psychosocial functioning of both the individual and their families (Blok et al., 2007; Primeau et al., 2000; Sicherer et al., 2001). For example, food allergy may result in restriction of social activities (including eating outside the home, attending social events, more time expended in shopping for food) and experience of anxiety (Gowland, 2001).

Hypoallergenic foods are currently being developed (for example, through application of genetic modification), which could facilitate food avoidance and therefore improve the quality of life of food allergic consumers (Hoffmann-Sommergruber and SAFE-consortium, 2005; Lorentz et al., 2006). Several examples exist of genetically modified foods with reduced levels of allergenic proteins, such as rice (Nakamura and Matsuda, 1996), soybean (Herman et al., 2003), apple (Gilissen et al., 2005), peanuts (Dodo et al., 2005), and tomato (Lorentz et al., 2006). However, genetic modification is not the only approach which can be applied to the development of hypoallergenic foods and ingredients. Other novel processing techniques, such as high pressure processing or extreme heat application, may reduce the allergenicity of problematic foods and ingredients (Davis et al., 2001). Novel ‘natural foods’ and food ingredients are new to and have no history of safe use in the European Union. Both “technological” (Davis et al., 2001) and ‘natural novel’ foods (Lucas et al., 2005) may exhibit reduced allergenicity and therefore they may contribute to allergy mitigation. This chapter discusses three types of novel foods: genetically modified novel foods (GM) , technological novel foods and ‘natural’ novel foods. All three types can be hypoallergenic, but they also might introduce new allergic responses by inserting novel proteins into the food chain (Taylor and Hefle, 2001).

The question arises as to whether these various novel products are acceptable to both food allergic consumers (Frewer et al., 1997; Schenk et al., 2008) and relevant

actors in the food chain (Putten et al., 2006). If novel hypoallergenic foods are to result in improvements to public health, they must be accepted by both stakeholders and consumers (Cornelisse-Vermaat et al., 2008b). As stakeholder opinion is likely to influence societal debate about the risks and benefits of these novel food products, understanding the opinions of key stakeholders is highly relevant (Putten et al., 2006). Consumer perceptions regarding the risks and benefits of novel foods are also likely to influence acceptance or rejection of specific products (Miles and Frewer, 2001). The introduction of genetically modified foods into the European food chain has resulted in consumer negativity in the past (for example, see Frewer at al, 2004). The introduction of novel foods as a solution to food allergy problems may not be universally accepted by non-allergic consumers, who will not directly benefit from their introduction (Schenk et al., 2008). Furthermore, whilst novel foods with reduced allergenicity have some benefits for food allergic consumers as the introduction of novel foods might reduce or alleviate the allergenicity of problematic ingredients (Gilissen et al., 2005; Kuiper et al., 2002), there is also the potential risk that new proteins are introduced into the human food chain, which may increase allergic reactions, or introduce new allergic responses (Taylor and Hefle, 2001).

If novel foods are to be included as part of a food allergy as allergy mitigation strategy, acceptance by food chain actors and consumers is required. It is generally believed that experts think about food risks differently from members of the public (Fife-Schaw and Rowe, 1996; Krystallis et al., 2007). Experts and regulators often use technical risk assessments to determine acceptable safety levels in general and food allergy in particular (Taylor and Hefle, 2001) whereas consumer decision making is, in part, based on broader societally relevant factors of concern, such as the extent to which an individual perceives the risk of a hazard to be uncertain, dreadful, potentially catastrophic, uncontrollable, equitable distributed and presenting risks to future (Frewer et al., 2004; Slovic, 1999). Optimising a public health policy regarding the introduction of novel hypoallergenic foods is contingent on both stakeholder and consumer acceptance of novel foods and associated production processes where relevant.

The aim of this chapter is to gain insight in the potential impact of hypoallergenic novel foods on public health issues associated with food allergy, as well as potential barriers to their introduction, by comparing the perspectives of both food allergic consumers and relevant actors in the European food chain. The views of key stakeholders must be systematically evaluated in order to predict potential societal responses to novel hypoallergenic foods. Important stakeholders include food industry, public health authorities, scientists and health professionals. Acceptance of novel hypoallergenic foods is contingent on acceptance by both stakeholders and consumers.

Stakeholder behaviour regarding novel foods should be relevant to consumer opinions and expectations.

It should be noted that the research is exploratory in nature and the intention was not to test a particular theoretical perspective, but to begin to gather knowledge about which risks, costs and benefits associated with novel foods and allergies may inform the societal debate about their introduction in the future. The research aims to answer the question as to whether novel foods can be used as allergy mitigation strategy, which is contingent on both stakeholder and consumer assessments of the hypoallergenic foods themselves, as well as the production processes used to develop them in the case of potentially controversial food technology applications.

### 3.2 Methodology

In the description of methodology that follows, the term stakeholder will be used to describe all stakeholders other than consumers, for reasons of clarity. The *stakeholder analysis* aimed to identify stakeholder opinions about novel foods applied as part of a food allergy mitigation strategy. Stakeholders included different food chain actors who have interests in the development and introduction of novel foods, or food allergies, or both as part of their professional lives These stakeholders answered questions during the course of semi-structured qualitative interviews. Representatives from these stakeholder groups were recruited through established contacts, based on their (hypothesised) expertise. A cascade methodology was applied, such that stakeholder recommendations for further stakeholders to include in the analysis were utilised in further recruitment. Further recruitment of stakeholders into the study ceased when the information obtained during the interviews became theoretically saturated i.e. when no further new information was obtained from additional interviews. In total 16 European stakeholder representatives were interviewed: three health professionals, three food industry representatives, three public health authority representatives, three scientists, two representatives from non-governmental organisations and two from patient organisations. These stakeholder categories were selected in line with those identified in a previous stakeholder analysis relevant to food allergy issues (Miles et al., 2006b). The list of questions was sent to stakeholders in advance, to allow participants to prepare for the interview, and to consult with colleagues if appropriate. All stakeholder representatives were recruited within Europe. The interviews, conducted by the same interviewer, took place between February 2005 and February 2006, and were conducted by telephone or in person when the travel distance permitted. The interviews were recorded for transcription purposes. Respondents were given the opportunity to comment on the transcript of the interview before further analysis took place.

Table 3.1 Demographic characteristics of the focus group participants

| Characteristics | Category | N |
|---|---|---|
| Gender | Male | 1 |
| | Female | 18 |
| | *Total* | 19 |
| Age | 17-24[9] | 4 |
| | 25-34 | 5 |
| | 35-44 | 7 |
| | 45-54 | 0 |
| | 55-64 | 2 |
| | >65 | 1 |
| | *Total* | 19 |
| Working status | Full-time | 5 |
| | Part-time | 4 |
| | Pensioner | 2 |
| | Student | 4 |
| | Homemaker | 1 |
| | On disability allowance | 1 |
| | Different | 2 |
| | *Total* | 19 |
| Education level | Low | 1 |
| | Medium | 7 |
| | High | 11 |
| | *Total* | 19 |
| Allergy[10] | (Pea)nuts | 11 |
| | Egg | 1 |
| | Milk | 5 |
| | Shellfish | 3 |
| | Fish | 1 |
| | Soy | 3 |
| | Celery | 1 |
| | Sesame seed | 2 |
| Diagnosis[11] | General practitioner | 3 |
| | Specialist | 9 |
| | Self | 8 |
| | Other (homeopath/ kinesiotherapist) | 4 |

In order to compare the views of food chain actors with food allergic consumers, additional research using focus group methodology was conducted using food allergic consumers. Considering that the topic of discussion, novel foods, is new to most food allergic consumers, focus group discussions were the most suitable method for data

[9] Parental permission to participate to the focus group discussion was obtained for the 17 year old participant.

[10] Multiple allergies in one person are calculated as separate allergies.

[11] Multiple diagnosis for one person are calculated as separate diagnosis.

collection. This method allowed participants to develop and explore their opinions on novel foods through group interactions under the guidance of a moderator more effectively than using semi-structured interviews. To determine the opinions of food allergic consumers, three focus group discussions were held in January and February of 2007 in Wageningen, The Netherlands. Participants were recruited *via* a newspaper advertisement, message boards in supermarkets, and an announcement on the intranet message board of Wageningen University and Research Centre (WUR). As for the stakeholders, a cascade recruitment methodology was used, such that participants were asked to invite other food allergic of food intolerant consumers to the focus groups. Between five to eight food allergic or food intolerant consumers participated in each focus group, which were lead by the same moderator. One focus group included only anaphylactic food allergic consumers, whereas the other two focus groups were comprised of food allergic consumers, who experienced less severe food allergic reactions (see table 3.1 for demographic and diagnostic analysis).

The focus group discussions utilised the same protocol, which was approved by Wageningen University ethical committee. After an introduction round, a free association task followed during which the participants wrote down the three most important food allergy problems on three pieces of paper. This resulted in an overview of the food allergy problems according to the participating food allergic consumers. The participants then discussed what should be to improve the food allergy problems they had previously identified. These problems were used to start the discussion about novel foods. Prior to the discussion, novel foods were defined and examples were provided. The focus groups lasted approximately 90 minutes. After participation in the focus group, participants received a 20€ gift certificate. Following the agreement of participants, the focus group discussions were audio recorded for transcription purposes.

### 3.3 Results

This section presents the results from both the stakeholder analysis and the focus group discussions. First the results from the stakeholder analysis are presented, followed by the presentation of the focus group discussion. Comparison of the stakeholder and consumer views is made, and some conclusions regarding the overall acceptability of novel foods as mitigation strategies for food allergy discussed.

Stakeholder analysis

All stakeholders perceived some potential contribution from novel foods to the prevention of food allergy occurrence. An important barrier to the introduction of such novel foods related to practical implementation.

Health Professional 2[12]: *"I think the potential is perhaps when modifying the protein structure of food, so that the allergenic part is eliminated. It's an exciting idea. And I think that it could help in theory. In practice it may be difficult, because it may be hard to identify a genetically modified, and therefore safe, food compared to the original version."*

Some stakeholders stated that hypoallergenic novel foods may provide an alternative for allergenic food products and ingredients and offer a wider food choice to food allergic consumers. However, stakeholders stressed that consumer acceptance of these novel foods was an important determinant of whether their introduction would be successful or not.

Scientist 3: *"Well, I think if you could introduce novel foods that are not going to cause an allergic reaction, so that people who have allergy can have a wider choice so that there might be an alternative to them for the food they are allergic to, then that might be something that would improve their quality of life. But I think what you need to do is to make sure or to look into whether people with food allergy would be prepared to eat novel foods."*

The stakeholders tended to associate novel foods with solutions to the problem of food allergy, although potential increases in food allergy incidence were also identified. The latter were mainly theoretical, and have not yet been observed in practice: for example, stakeholders postulated that novel foods can contain existing or novel allergens or that novel processing techniques may change protein folding revealing new epitopes, which are the binding sites for IgE.

*Food Industry representative 1: "Maybe these genes can produce a protein which causes another reaction [to that] expected."*

While it may be technically possible to develop novel foods that are hypoallergenic or which do not provoke an allergic reaction in some food allergic consumers, some stakeholders did not consider the introduction of hypoallergenic novel foods as a realistic option throughout the relevant food chains. This was because only a minority of the population is affected by specific food allergies. In addition, the introduction of novel proteins into the food chain in itself may be problematic, as consumers may develop allergies to the novel proteins following long-term effect of exposure. In particular, natural

[12] The number refers to a specific individual in this stakeholder group.

novel foods were described as actually causing new problems, as they cause allergic reactions.

*Public Health Authority representative 1: "Kiwi is a good example of a natural novel food that can be allergenic."*

There may be unexpected effects that cannot be foreseen at the present time. For example, some stakeholders thought the introduction of novel foods could result in more allergies, increased allergenicity of the food or allergenic gene expression in the case of genetic modification if new or existing allergens are introduced into the human food chain.

> Health Professional 2: *"Well, I think novel foods could increase problems if there is not enough legislation or testing of them… in theory that can cause problems as well."*

Other stakeholders thought existing regulatory systems and testing methods were sufficient to protect consumers from the risks of novel foods.

> Public Health Authority representative 2: *"Yes, potentially they could increase problems, but that of course relies on the risk assessment that we do. I think the regulation is so strict that we will not allow products [to be introduced] when we are in doubt. But of course you could imagine some kind of technological change of the food, which we cannot predict that enhances allergenic potential of the food."*

In summary, most stakeholders believe that novel foods can, in theory, contribute to a solution for the food allergy problems they described, because they are potentially less allergenic and therefore may represent a safe alternative for allergenic food consumers. Natural novel foods are only a good alternative when the products are proven safe, but initially stakeholders considered them more as a cause of consumer's food allergy problems. The stakeholders also mentioned some potential problems when novel foods are introduced, such as consumers who develop allergies to the novel proteins in novel foods. Of course, novel foods can only have these benefits if consumers are willing to buy them.

<u>Focus group discussions</u>

Food allergic consumers reported that the *best* way to influence the food allergy problems would be through reduction or elimination of the symptoms of food allergy. If food allergic consumers experienced mild symptoms, or no symptoms, after eating foods to which they are allergic, they would not need to invest so much effort in avoiding the consumption of allergenic proteins. Shopping would take less time, and eating outside the home would be less troublesome, as measures would not be needed to prevent accidental exposure to allergens. Social restrictions would also be reduced. Whilst many

participants expressed the view that they would be in favour of novel hypoallergenic foods being developed and commercialised doubts were expressed regarding whether the novel foods really would be less allergenic. This illustrates that participants in the focus groups doubted whether novel foods potentially reduced their allergenicity. Doubts were also expressed more directly.

> [13]B1: *"I do not believe this at all."* and *C5: "I do not believe that [the food industry] they would put the consumer's interest first. "*

Consumers perceived that novel foods could only be used for allergy reduction when all food ingredients are replaced across all food chains. For example, if a less allergenic variety of wheat could be found, this could be beneficial for consumers who are intolerant of gluten because this would allow them to consume products that contain wheat, but only if the new variety was used in all products containing wheat. However, this view was expressed that such comprehensive introduction of the new variety across all food chains may not be feasible. In addition, the food allergic consumers included in the study indicated that they would only trust novel hypoallergenic novel foods to be safe to consume following positive experience with specific products.

> B7: *"You just have to try them. If you never try something new, you will also never find a solution to your problem."*
>
> *B6: "I trust that these foods can be further developed and that they can provide substantial mitigation."*

One difference between people with immediate allergic symptoms and people with symptoms that appear later, (for example, as in the case of food intolerance such as celiac disease) is that the latter are less willing to experience the potentially beneficial effects of the novel foods. The reason for this is that those consumers could suffer intestinal damage before they notice that they still react to the novel wheat. People with a severe food allergy stated that they would not want to consume novel hypoallergenic foods. Thus the perceived severity of the allergic reaction experienced by specific consumers influences the likelihood that consumers will try novel hypoallergenic foods. In addition, reducing the allergen content of a food product was thought not be sufficient for consumers who respond to small amounts of the problematic food. This led to the conclusion that food allergic consumers differed in their opinion depending on the specific food allergy and on the sensitivity (threshold level) of the allergic individual. In addition, consumers indicated that the easier it was to avoid consumption of a particular

[13] The three different focus group discussions are indicated with either, A, B or C. The number refers to a specific individual participating in one of these focus group discussions. For example, consumer C5, refers to food allergic consumer number 5 in the third focus group discussion.

food, the less was the perceived need to develop substitutes in the form of novel foods. For example, there was more acceptance of products that are often used as an ingredient such as milk.

> *C4: "I can imagine that using a novel food as substitute for a product that is an ingredient for many other products would be better than when it substitutes a product that is consumed directly."*

However, consumer demands for sensory experience should not be neglected. Some food allergic consumers stated they would like to eat certain foods again.

> A5: *"It would be great if I could eat red beets again."*

This implies that care should be taken to avoid changing the sensory characteristics of a food if allergenicity is reduced. Another advantage perceived by consumers was that by consuming these novel foods that contain less allergens, the consumer would be exposed to fewer allergens, which would prevent or delay the development of new allergies.

Food allergic consumers also identified problems with the labelling of novel foods when they are used as an ingredient in other products, as they would have to look on the package to identify what type of ingredient (traditional or novel) was used. The problem would even be exacerbated in the case of 'may contain labelling', (Cornelisse-Vermaat et al., 2008a; Cornelisse-Vermaat et al., 2008b) as it would be even more difficult to estimate what the risk is of the product containing traces of the allergenic ingredient actually is, as one could not estimate whether the potential contamination is from traditional or hypoallergenic ingredients, as well as the issue of whether the novel foods would be more expensive.

> B4: *"Then you get labelling that says: 'this product has been produced in a factory where allergenic peanuts are processed.'…and if it is possible to separate the allergenic peanuts from the non allergenic peanuts, then you will pay ten Euros for a package of non allergenic peanuts."*

The focus group participants worried about the changes that genetic modification would cause to the product as a whole.

> A4: *"I am afraid that the peanut will change in so many ways that it is no longer a peanut."*

To summarise, food allergic consumers would be in favour of novel hypoallergenic foods being developed and commercialised. However, they do have doubts about whether the novel foods would be less allergenic. Consumers perceived that novel foods could only be used for allergy reduction when all food ingredients are replaced across all food chains completely. Food allergic consumers with immediate symptoms are more willing to experience the potential benefits of novel foods than consumers with symptoms that

appear later. Another advantage of hypoallergenic novel foods according to the food allergic consumers is that these novel foods could prevent or delay the development of new allergies because the consumers are exposed to reduced levels of allergenic proteins.

### 3.4 Discussion

The results of the study suggest that both food allergic consumers and experts associate advantages and disadvantages with the introduction of novel hypoallergenic novel foods and their utility as part of a risk management strategy for food allergy. Food allergic consumers considered the inappropriate immune response to be the main cause of the food allergy problems. They find it unlikely that novel foods will contribute to a cure for food allergy. Only one stakeholder had same opinion. However, both food allergic consumers and experts could see some contribution of novel foods to allergy mitigation. Novel foods could have some mitigating influence on allergy symptoms by limiting the exposure to allergens, the “tertiary prevention of food allergy” (Zeiger, 2003). An acceptable example might be when a natural hypoallergenic variant of an allergenic food exists which can introduced into the food chain. Focus group participants did express some doubts about whether novel foods could really be less allergenic. In addition, the consumers stated that, if novel hypoallergenic foods are to be accepted by consumers, the taste and price need to be similar to their traditional counterparts. The experts mentioned that for novel foods to be successfully applied as an allergy mitigation strategy, they need to be accepted by consumers. The experts did not specify the requirements that need to be met for food allergic consumers to accept novel foods.

The food allergic consumers did not express a preference for more natural types of novel food over genetically modified novel foods. The perceived benefits and the influence on daily life was more important to them than production process *per se*. This is in contrast with the quantitative analysis provided by Schenk et al. (2008) who report that food allergic consumers are less tolerant of novel food processing applied to the development of hypoallergenic foods if the allergic symptoms are mild (Schenk et al., 2008). This may, in part, be due to the emphasis of the research presented here, which did not seek to examine how food allergic consumers make trade-offs between perceived risk and benefit of production technologies, but rather “framed” the research in the context of specific benefits to food allergic consumers. The stakeholders thought it more likely that genetically modified and technological novel foods can contribute to food allergy mitigation than natural novel foods.

Limitations of the research

The results cannot be extrapolated to the general population because of small sample sizes. In particular, further research using quantitative methodology and larger, more representative samples of food allergic and food intolerant consumers, is required. The question of acute and chronic negative responses to foods, and how this interacts with acceptance of novel foods also required further research. Finally, the issue of societal acceptance of hypoallergenic ingredients produced by novel food processing technologies must be addresses in the context of general consumer acceptance, not just that of food allergic consumers. However, the results are indicative of potentially important factors determining societal acceptance of novel hypoallergenic foods in the future.

### 3.5 Conclusions

Both consumers and stakeholders expressed some enthusiasm for the introduction of truly hypoallergenic novel foods, with the caveat that evidence was required to assess whether the novel products were reliably hypoallergenic and still have all the same product characteristics as the “traditional” allergenic product. As well as rigorous risk assessment, post market surveillance would be required to test whether the novel products were indeed hypoallergenic and could be consumed by all consumers who were allergic to them. The need for “guarantees” of hypoallergenicity increased with the severity of the allergic response following consumption.

In addition, food allergic consumers feared that eventually they would develop an allergy to the novel foods because their immune system is the cause of the food allergy. The stakeholders indicated that some benefits of novel foods for food allergic consumers could be identified, although systematic risk assessment would be required prior to any market introduction. It is notable that both consumers and stakeholders questioned whether the novel foods were truly less allergenic. This again indicates the need for rigorous (allergy) risk assessment of hypoallergenic novel foods, together with an appropriate regulatory structure developed to optimise consumer protection associated with potential introduction of novel hypoallergenic foods (Putten et al., submitted). Whilst the results suggest that novel hypoallergenic foods have the potential to increase the dietary variation available to food allergic consumers, consumers expressed the view that a “cure” for food allergy is preferred over substitution of existing foods with hypoallergenic allergenic counterparts.

Societal acceptance of novel hypoallergenic foods will depend not only on the fact that the novel foods are hypoallergenic, but also on the severity of the allergic

response should it occur. Whilst societal demand for foods used as ingredients, as opposed to whole foods which are easily avoided by consumers, is a priority for all participants in the study, their widespread inclusion in the food chain will be dependent on rigorous demonstration of their safety for all food allergic consumers. This is particularly important given that differences in severity of allergic response (for example potentially fatal reactions to peanut proteins). Finally, the introduction if novel production processes such as genetic modification of foods was not problematic for consumers in this study, However the widespread introduction of genetically modified ingredients (as opposed to whole foods) still requires further consideration, as they will be consumed by non-food allergic consumers who will not derive personal benefits from their consumption.

**Acknowledgements**

The authors would like to thank all stakeholders who were interviewed and the food allergic consumers who participated in the focus groups. This research has been done as part of a PhD project funded by the Allergy Consortium Wageningen, The Netherlands.

# Chapter 4

# Consumer attitudes towards novel foods as allergy management strategy

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To be submitted

**Abstract**

Food allergies may have a negative impact on the quality of life and the economic functioning of people who suffer from them, as well as the society in which they live. Food allergy is defined as inappropriate immunological reaction to normally harmless food components. Hypoallergenic novel foods may improve quality of life of food allergic consumers when they are accepted by both food allergic and non-allergic consumers. This study identifies different consumer groups depending on their attitudes towards the risks and benefits of novel foods and their acceptance. In addition, the influence of information about the impact of food allergy on the lives of food allergic consumers, and about the potential benefits of novel foods on novel food acceptance among non-food allergic consumers is identified. A cluster analysis was used to form groups of similar consumers. To test the influence of information on novel food acceptance among non-food allergic consumers an experiment was conducted.

The results showed that four distinct consumer groups could be identified based on their hypoallergenic novel food attitudes and acceptance. The group that was least likely to accept hypoallergenic novel foods, was the group with most food allergic consumers. This indicates that the application of novel foods as an allergy management strategy is complicated because many of the consumers who are supposed to experience benefits of these novel foods are less likely to use the novel foods. Information about the impact of food allergy on the lives of food allergic consumers, and about the potential benefits of novel foods appeared to improve acceptance of these novel foods among non-food allergic consumers.

## 4.1 Introduction

Food allergy, an inappropriate immunological reaction to normally harmless food components, affects 5-8% of children and 1-2% of adults (Buttriss and Schenker, 2002; Rona et al., 2007; Sicherer et al., 2001). Food allergies may have a negative impact on the quality of life (Fernandes-Rivas and Miles, 2004) and the economic functioning of people who suffer from them, as well as the society in which they live (Fox et al., in press; Miles et al., 2005; Voordouw et al., 2009). Quality of life is 'the individual's perception of their position of life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns' (WHO, 1993). Caregivers of a food allergic child could develop some degree of anxiety and protectiveness given the potential for severe reactions and the lack of control (real or perceived) in some food consumption situations (Bollinger et al., 2006; Primeau et al., 2000). Food allergy potentially affects meal preparation activities in the home, social activities (for both parents and children), may be associated with anxiety, and have a detrimental affect on school attendance. The time and effort that it takes to provide a safe environment for food allergic children has potential to cause a significant impact on daily life. Children who suffer from more than two food allergies report lower quality of life scores, a similar experience to that of their parents.

The only effective treatment for food allergy available at the time of writing is for food allergy sufferers to avoid the problematic foods (Ortolani and Pastorello, 2006) which may limit food choices, or social and travel opportunities (Oude Elberink, 2006; Sicherer et al., 2001). They may even avoid situations, which are potentially harmful. This means that food allergic consumers may have to alter their style of living, which may have a negative impact on the families of food allergic consumers' (Bollinger et al., 2006).

Various approaches to solving the problems associated with food allergy are currently under development. A prominent example is the development of *novel hypoallergenic foods*, developed for example through the application of novel processing technologies such as genetic modification, more traditional techniques such as selective breeding, or through introduction of novel foods not hitherto used in the food chain (Hoffmann-Sommergruber and SAFE-consortium, 2005; Putten et al., 2006; Schenk et al., 2008) In the context of the European regulatory framework, novel foods are foods or food ingredients with no consumption history in the European Union. The absence of a history of safe use can be the result of: (1) genetic modification (GM) of the food or production of the food using, genetically modified organisms, (2) novel processing techniques, or (3) the food being novel to the European Union.

The introduction of novel foods as an approach to food allergy management may be ambiguous. On one hand, there is the potential risk that new proteins are introduced into the human food chain together with the novel foods (Taylor and Hefle, 2001), which may increase allergic reactions. Against this, there are the potential benefits for food allergic consumers as the introduction of novel foods might reduce their allergenicity (Dodo et al., 2008; Kuiper et al., 2002; Moseley, 2001). However, the extent to which consumers accept these novel foods also needs to be understood if they are to be introduced into the food chain. Successful commercialisation of hypoallergenic products may be contingent on the extent to which consumers perceive benefits to be associated with hypoallergenic novel foods. It can be expected that food allergic consumers are more likely to accept novel foods than non-food allergic consumers because hypoallergenic novel foods may have benefits for consumers with a food allergy. In addition, non-food allergic consumers who are informed about the benefits of hypoallergenic novel foods could be more likely to accept novel foods than non-food allergic consumers without such information. Perceived benefits associated with food production technologies such as GM may be important in determining public acceptance of both the technology and its products. However, public reactions will be determined by a combination of risk and benefit perceptions (Rowe, 2004). Other factors, such as perceived "naturalness" of food products, and perceptions of the "need" for new products, may also determine acceptance (Tenbült et al., 2005). People's preference for "naturalness" appears to be greater for food compared to other sectors, for example for medicines (Rozin et al., 2004). This information is important for the developers of low allergen food products (food industry and food scientists) and policy makers to ensure that the needs of the allergic consumers are met, benefiting these consumers and the food industry (Miles et al., 2006a). However, the introduction of novel foods and ingredients may raise other individual and societal concerns (Frewer et al., 2004), which may reduce consumer acceptance. In addition, the extent to which hypoallergenicity is certain may influence consumer acceptance (Schenk et al, in preparation). Consumer attitudes towards novel consumer products need to be identified if the use of novel foods is to be accepted as a strategy for food allergy management.

The aim of the research presented here was to identify different consumer groups based on attitudes towards the application of hypoallergenic novel foods as food allergy management. Additionally, the influence of information about the impact of food allergy on the lives of food allergic consumers, and about the potential benefits of novel foods on novel food acceptance among non-food allergic consumers is identified.

## 4.2 Methodology

### 4.2.1 Participants and research design

First, both food allergic and non-food allergic consumers were classified based on novel food attitudes and novel food acceptance. Data were collected using a panel of food allergic and non-food allergic consumers. The food allergic consumers were selected using the selection questions presented in annex A. Respondents who reported an allergy to peanut, nut, fruit, fish or shellfish, and had avoided these foods for more than one year, were invited to participate in the study. Data were also collected from a panel of Dutch non-food allergic consumers who were excluded from the study as if they self-reported experiencing a food allergy. Representativeness of the panel for the Dutch population was derived from quota sampling on the basis of region, gender, household income, and age. Table 4.1 shows the demographic characteristics and reported food allergies of the sample[14]. In total 438 respondents participated in the research: 199 consumers who self-reported experiencing a food allergy, and 239 consumers who did not report having a food allergy. There are no missing data.

After the consumer groups have been identified, an experiment was conducted with the non-food allergic consumers to test whether information about the impact of having a food allergy and about novel foods benefits influences acceptance of these hypoallergenic novel foods. To test this a two-by-three experimental design was used. The non-food allergic consumers were randomly divided into two groups. One group received information about the impact of having a food allergy on daily life and about novel foods and their benefits, the other group received neutral information about food in general. (See annex B and C for the information that was provided to the two groups of non-food allergic consumers.) Both groups answered questions about three types of hypoallergenic novel foods.

[14] It should be noted that the allergy prevalences in this table do not reflect the range and prevalence of food allergies experienced by the food allergic population in the Netherlands. Respondents were selected on the basis having a nut allergy, a shellfish allergy or a fruit allergy. This was done to ensure larger numbers of respondents with similar allergies to make statistical comparisons possible.

Table 4.1 Demographic characteristics of the sample

| Characteristics | Category | Food allergic consumers N (%) | | Non-food allergic consumers N (%) | |
|---|---|---|---|---|---|
| Gender | Male | 47 | (23.6) | 116 | (48.5) |
| | Female | 152 | (76.4) | 123 | (51.5) |
| | Total | 199 | (100) | 239 | (100) |
| Age | 18 – 24 | 11 | (5.5) | 15 | (6.3) |
| | 25– 34 | 33 | (16.6) | 38 | (15.9) |
| | 35– 44 | 47 | (23.6) | 59 | (24.7) |
| | 45 – 54 | 57 | (28.6) | 46 | (19.2) |
| | 55 - 64 | 32 | (16.1) | 38 | (15.9) |
| | >65 | 19 | (9.5) | 43 | (18.0) |
| | Total | 199 | (100) | 239 | (100) |
| Working status | Full-time | 67 | (33.7) | 93 | (38.9) |
| | Part-time | 55 | (27.6) | 69 | (28.9) |
| | Unemployed | 5 | (2.5) | 3 | (1.3) |
| | Pensioner | 19 | (9.5) | 36 | (15.1) |
| | Student | 3 | (1.5) | 6 | (2.5) |
| | Homemaker | 28 | (14.1) | 20 | (8.4) |
| | On disability allowance | 17 | (8.5) | 8 | (3.3) |
| | Other | 5 | (2.5) | 4 | (1.7) |
| | Total | 199 | (100) | 239 | (100) |
| Education level | Low | 48 | (24.1) | 91 | (38.1) |
| | Medium | 77 | (38.7) | 89 | (37.2) |
| | High | 74 | (37.2) | 59 | (24.7) |
| | Total | 199 | (100) | 239 | (100) |
| Household income | <700 | 47 | (23.6) | 54 | (22.6) |
| | 700 -1500 | 64 | (32.2) | 76 | (31.8) |
| | 1500 – 2300 | 48 | (24.1) | 58 | (24.3) |
| | 2300 – 3100 | 6 | (3.0) | 17 | (7.1) |
| | 3100 – 4100 | 5 | (2.5) | 3 | (1.3) |
| | >4100 | 1 | (0.5) | 0 | (0) |
| | Undisclosed | 28 | (14.1) | 31 | (13.0) |
| | Total | 199 | (100) | 239 | (100) |
| Allergy[15] | Peanut | 51 | (25.6) | | |
| | Nut | 102 | (51.3) | | |
| | Milk | 31 | (15.6) | | |
| | Egg | 10 | (5.0) | | |
| | Wheat | 7 | (3.5) | | |
| | Soy | 12 | (6.0) | | |
| | Sesame seed | 13 | (6.5) | | |
| | Fish | 20 | (10.1) | | |
| | Shellfish | 95 | (47.7) | | |
| | Celery | 6 | (3.0) | | |
| | Fruit | 69 | (34.7) | | |
| | Vegetables | 18 | (9.0) | | |
| | Other | 37 | (18.6) | | |
| | Total | 471 | | | |

[15] Multiple allergies on one person are calculated as separate cases.

### 4.2.2 Methods and Materials

Surveys were administered in September 2008 by a social research agency. Consumers' risk and benefits perceptions, and acceptance of hypoallergenic novel were measured. Food allergic consumer benefit perceptions were measured with the statements: 'the benefits of hypoallergenic novel foods for me personally are…', and 'the benefits of hypoallergenic novel foods for the average person in the Netherlands are…' Food allergic consumer risk perceptions were measured with the statements: 'the risks of hypoallergenic novel foods for me personally are…', and 'the risks of hypoallergenic novel foods for the average person in the Netherlands are…'. Both risk and benefit perceptions were measured on a 7-point Likert scale where 1 indicates low benefit/risk perceptions and 7 indicates high benefit/risk perceptions. Acceptance of novel foods was measured with the statements: 'I would buy genetically modified novel foods with benefits for my allergy if they are similar in taste and price as conventional products', 'I would buy technological novel foods with benefits for my allergy if they are similar in taste and price as conventional products', and 'I would buy natural novel foods with benefits for my allergy if they are similar in taste and price as conventional products'. The measure for GM attitudes in general was previously developed and validated by Frewer et al. (Frewer et al., 1997). This GM attitude measure contained 17 items, which included "risky", "long term effects", "dangerous", "harmful", "personal worry", "tampering with nature", "personal objections", "creation of inequalities", "negative welfare effects" "unnatural", "beneficial", "advantageous", "necessary", "important", "progressive" "unethical", and "immoral". These items were translated into Dutch. The translated items were tested in the pilot study. Acceptance was measured on a 7-point Likert scale where 1 indicates no acceptance and 7 indicates very high acceptance. In each questionnaire the GM attitude measure items were the last to be completed. The order in which the items were presented was randomised. Before completing the GM attitude measure items, respondents were given a definition of GM, previously used by Frewer et al. (1997). The GM definition was translated into Dutch as well.Non-food allergic consumer benefit perceptions were measured with the statements: 'the benefits of hypoallergenic novel foods for food allergic consumers are…', and 'the benefits of hypoallergenic novel foods for the average person in the Netherlands are…' Non-food allergic consumer risk perceptions were measured with the statements: 'the risks of hypoallergenic novel foods for food allergic consumers are…', and 'the risks of hypoallergenic novel foods for the average person in the Netherlands are…' Both risk and benefit perceptions were measured on a 7-point Likert scale where 1 indicates low benefit/risk perceptions and 7

indicates high benefit/risk perceptions. Non-food allergic consumer acceptance of novel foods was measured with the statements: 'Genetically modified novel foods with benefits for food allergic consumers should be made available in stores', 'Technological novel foods with benefits for food allergic consumers should be made available in stores', and 'Natural novel foods with benefits for food allergic consumers should be made available in stores'. In addition to the novel food acceptance also GM attitudes in general were measures. GM attitudes of the non-food allergic consumers were measured using the same scale as for the food allergic consumers, previously developed by Frewer et al. (1997).

### 4.2.3 Data analysis

Ward's hierarchical clustering method was used to identify groups of consumers for which the individual differences between the groups dominate the differences within the groups (Kornelis et al., 2007). The novel food acceptance items, the risk and benefit items, and the aggregated scores on the GM scales served as a classification basis. An optimal number of consumer groups was based on the agglomeration schedule following inspection of the results. Subsequently the clusters "were fine-tuned" using the non-hierarchical K-means clustering method. Significant differences between these different consumer groups regarding the descriptive and classification variables were assessed by means of F-tests.

The data were analysed using SPSS. Factor analysis was used to derive a measure for GM acceptance. The rotated (Oblimin, correlation -0.52) two factor solution (PCA) explains 65.5% of the variance. These two components have Eigenvalues higher than 1. The first component, which explains 55.1% of the variance loads heavily on "risky", "long term effects", "dangerous", "harmful", "personal worry", "tampering with nature", "personal objections", "creation of inequalities", "negative welfare effects", and "unnatural". This component could be labelled as "rejection". The second component explains 11,5% of the variance and loads heavily on "beneficial", "advantageous", "necessary", "important", "progressive" and also on "unethical" and "immoral". The loadings on "unethical" and "immoral" are negative. The second component could be labelled "acceptance". The third component has an Eigenvalue below 1. Therefore this factor is not taken into account. For further analysis the two aggregated factors for GM attitude have been used instead of the 17 items. Cronbach's α is 0.92 for the "rejection" factor and Cronbach's α is 0.90 for the "acceptance" factor.

## 4.3 Results

### 4.3.1 Consumer classification

A cluster analysis was performed to identify similar groups of consumers based on novel food attitudes and their acceptance of novel foods. Four different consumer groups were identified on the basis of the cluster analysis. The consumer groups differ significantly on the dependent variables that were used to distinguish the consumer groups. The variables used to cluster the consumers included the following: Individual novel food benefits and risks, general novel food benefits and risks, GM novel food acceptance, non-GM technological novel food acceptance, natural novel food acceptance, and two GM attitude measures). The consumer groups also differed from each other in terms of whether they reported having a food allergy or not. In addition, the consumer clusters were compared in terms of demographic factors (age, gender, education level, occupation, household income, and household size), but significant differences between the clusters were not identified for these variables.

Table 4.2 Mean ratings (standard deviation) of the significant classification variables

| | Pro novel food consumers | Benefit contingent consumers | Negative consumers | Uncommitted consumers | Statistics |
|---|---|---|---|---|---|
| Individual novel food benefits | 5.17 (1.49) [a] | 5.08 (1.44) [a] | 3.68 (1.52) [b] | 4.95 (1.12) [a] | F=14.38 df=3, 219 p<0.0001 |
| General novel food benefits | 3.74 (1.27) [a] | 4.60 (1.38) [b] | 3.91 (1.28) [a,b] | 3.49 (1.09) [a] | F=5.24 df=3, 219 p=0.002 |
| Individual novel food risks | 2.29 (0.94) [a] | 4.24 (1.09) [b] | 1.95 (1.05) [a] | 3.51 (1.13) [c] | F=44.36 df=3, 219 p<0.0001 |
| General novel food risks | 1.99 (0.90) [a] | 4.48 (0.82) [b] | 2.82 (1.18) [c] | 2.90 (1.16) [c] | F=35.04 df=3, 219 p<0.0001 |
| GM acceptance | 6.09 (0.87) [a] | 6.04 (0.89) [a] | 2.11 (1.07) [b] | 3.77 (1.09) [c] | F=195.45 df=3, 219 p<0.0001 |
| Technological acceptance | 6.25 (0.76) [a] | 6.00 (0.87) [a] | 2.34 (1.07) [b] | 4.64 (0.98) [c] | F=201.62 df=3, 219 p<0.0001 |
| Natural acceptance | 6.30 (0.73) [a] | 6.08 (0.86) [a] | 3.23 (1.40) [b] | 4.88 (0.93) [c] | F=104.89 df=3, 219 p<0.0001 |
| GM rejection | 3.76 (1.02) [a] | 4.04 (1.07) [a,b] | 4.31 (1.07) [b,c] | 4.68 (0.88) [c] | F=10.50 df=3, 219 p<0.0001 |
| GM acceptance | 4.52 (0.95) [a] | 4.11 (1.17) [a,b] | 3.29 (0.96) [c] | 3.62 (0.80) [b,c] | F=17.40 df=3, 219 p<0.0001 |

Note: All p values < 0.05 for all associated F-tests. The classification variables that share the same superscripts indicate cluster means that are not significantly different following Tukey's HSD test (all p values < 0.005)

Table 4.2 provides a summary of the mean ratings on the variables (measured on a 7-point scale) that differ significantly between the clusters. The first cluster consists

mainly of non-food allergic consumers. 48 (69.6%) Consumers in this cluster do no suffer from a food allergy. The second cluster also contains a majority of consumers without a food allergy. Sixteen (64.0%) consumers in this cluster do not have a food allergy. Cluster three consists mainly of food allergic consumers. Forty-five (80.4%) consumers in this cluster suffer from one or more food allergies. The fourth cluster consists mainly of non-food allergic consumers. In this cluster, forty-six (63.0%) of cluster members do not suffer from a food allergy. All consumers have a higher level of acceptance of "natural" novel foods compared to non-GM technological novel foods, which in turn is higher than their acceptance of GM novel foods. Based on these results the following profiles for the four consumer groups can be described:

1. **Pro novel food consumers (n=63).** Together with the "benefit contingent consumers", consumers in this cluster do not suffer from a food allergy (69.9% = 42 non-food allergic consumers) and tend to be positive about hypoallergenic novel foods. Consumers in this group perceive the benefits of hypoallergenic novel foods to be high and the risks to be low.
2. **Benefit contingent consumers (n=25).** The majority of the consumers in this cluster do not suffer from a food allergy (64.0%, 16 non-food allergic consumers). They perceive the individual benefits of hypoallergenic novel foods as high and the risks as average, compared to the consumers in the other clusters. These consumers report that they accept novel foods if they used as food allergy management strategy.
3. **Negative consumers (n=56).** The food allergic consumer group (with 80.4% = 45 allergic consumers) had the lowest scores on both individual novel food risks and benefits. Their willingness to buy the three types of novel foods was lower compared to even the non-food allergic consumers. In contrast to expectations, food allergic consumers were less likely to accept novel hypoallergenic foods than non-food allergic consumers. A possible explanation is that the food allergic consumers are more cautious regarding the consumption of new foods, adopting a risk avoidance strategy, even if these risks are not perceived to be high.
4. **Uncommitted consumers (n=73).** This group consisted of primarily non-food allergic consumers (63.0% = 46 non-food allergic consumers). These consumers perceive high levels of benefit perceptions and low levels of risk to be associated with novel foods, in a way similar to the "pro novel food and benefit contingent consumers", but they are less accepting of novel foods as a potential allergy mitigation strategy compared to consumers in this cluster.

### 4.3.2 Novel food acceptance among non-food allergic consumers

A total of 239 non-food allergic consumers answered questions about their acceptance of novel foods. One hundred and twenty one of these non-food allergic consumers received information about the impact of food allergy on the daily lives of food allergic consumers. The 118 non-food allergic consumers in the control group received neutral information about food. Both groups answered the same questions. Table 4.3 shows the means for acceptance of the three types of novel foods by consumers who had received information about the consequences of suffering from a food allergy and hypoallergenic novel foods, and consumers without such information. Acceptance was measured on a 7-point likert scale where 1 indicates no acceptance and 7 indicates very high acceptance.

Table 4.3 Acceptance of different types of novel foods in the experimental and control group

| | **Food allergy info group** | **Neutral info group** |
|---|---|---|
| | Mean (Std. dev) | Mean (Std. dev) |
| **Genetically modified novel foods** | 4.90 (1.73) [a] | 3.72 (1.70) [a] |
| **Non-GM technological novel foods** | 5.34 (1.47) [b] | 4.53 (1.46) [b] |
| **Natural novel foods** | 5.48 (1.29) [b] | 4.99 (1.42) [c] |
| **Novel foods (total)** | 5.24 (1.50) | 4.41 (1.53) |

The novel food types that share the same superscripts (column wise) indicate means that are not significantly different following Tukey's HSD test (all p values < 0.005)

The differences in novel food acceptance between consumers with information about the impact of food allergy on daily lives of food allergic consumers and consumers without such information were significant ($F=23.7$; $df=1, 237$; $p<0.0001$). This indicates that non-food allergic consumers who receive such information are more likely to accept hypoallergenic novel foods than consumers who do not receive such information. Analysis of variance for an effect of novel food type on acceptance shows a significant difference as well ($F=39.9$; $df=2, 236$; $p<0.0001$).

Information about food allergies and its consequences for people who suffer from them increased acceptance of novel hypoallergenic foods by non-food allergic consumers. Note that both consumers with information about food allergy and consumer without such information are more positive towards natural novel foods than non-GM technological novel foods. Similarly both groups are more accepting of non-GM technological novel foods than of GM novel foods. These findings imply that communication about the impact of food allergy on daily lives of people with a food allergy may help to accept the introduction of these novel foods by non-food allergic consumers who do not receive direct benefits from the novel foods themselves.

An interaction between the type of novel food and the information provision on the acceptance of novel foods was also observed (F=8.064, df=1,609, p=0.01). Figure 4.1 shows the acceptance of the three types of novel foods by the two groups of non-food allergic consumers. This effect indicates that the type of novel foods becomes less important in determining acceptance of novel foods when the benefits are communicated.

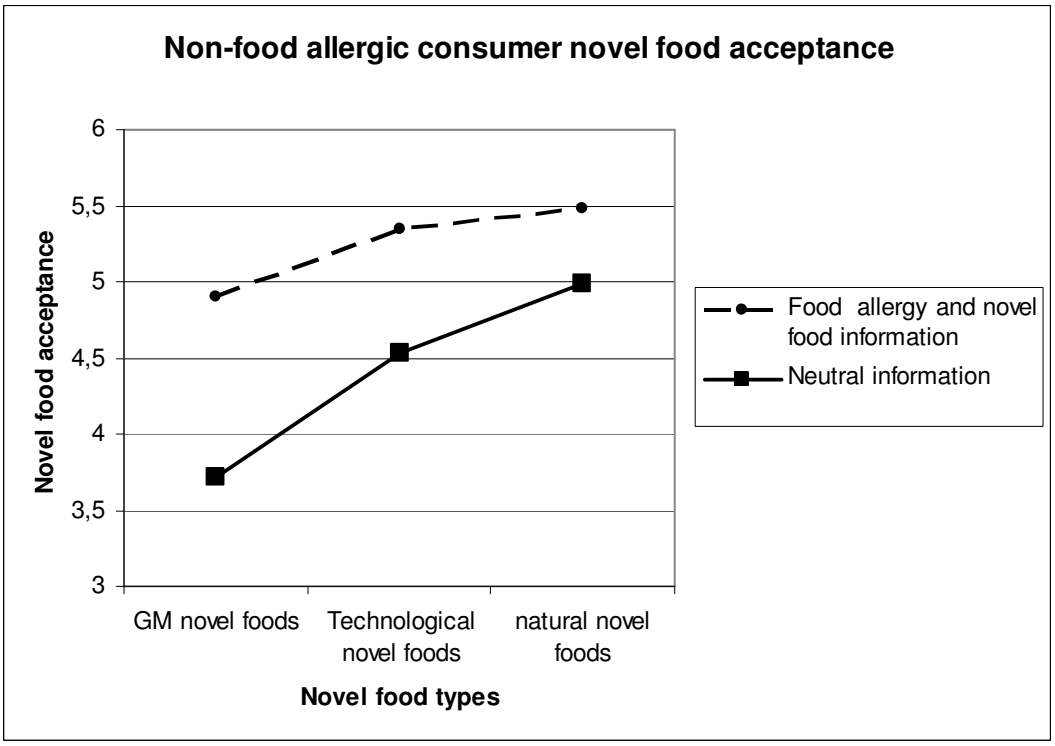


Figure 4.1 Non-food allergic consumer novel food acceptance

### 4.4 Discussion

The present study examined the consumer attitudes towards novel foods as food allergy management strategy. The empirical results indicate that four distinct consumer groups can be identified, which are characterised by different attitudes towards risks and benefits of novel foods, GM attitudes in general, and whether participants suffer from a food allergy. Twenty-five percent (56) of the consumers are somewhat negative about the application of novel foods as allergy mitigation strategy. Seventy-five percent of the consumers do not have a food allergy and their attitudes towards novel foods vary from being neutral (neither positive nor negative) about the applications of novel foods to being positive about them. Of the participants with the more negative attitudes, 45 were food allergic. Among the more positive consumers, 57 report a food allergy. These

results imply that the application of novel foods as an allergy management strategy is complicated because many of the consumers who are supposed to experience benefits of these novel foods are less likely to use the novel foods. Almost fifty percent (44.1%) of the food allergic consumers in the sample are reluctant to accept novel foods as an allergy mitigation strategy, although they perceive hypoallergenic foods to be associated with some benefits and low risks. This implies that universal replacement of potentially hypoallergenic foods in the food chain is unrealistic. However, the development of niche products to meet the demands of some food allergic consumers is indicated as possible way forward in the commercialisation of hypoallergenic foods, although further research is required to assess whether, for example, acceptance is inversely related to the potential severity of an allergic response should it occur (Schenk et al., 2008). In any case, naturally occurring hypoallergenic foods appear to be viewed more positively compared to those developed through application of emerging technologies.

A further point relates to developing a communication strategy about novel hypoallergenic foods. Some non-food allergic consumers appear to be more positive about novel hypoallergenic foods after they have received information about the potential problems experienced by food allergy sufferers, This implies that communication regarding the benefits of the novel foods might influence societal acceptance about novel foods in a positive direction, although this should also take account of differences in societal concerns about the potential use of different technologies on food production (Schenk et al., 2008).

Overall, consumer acceptance of novel foods is greater for those which occur naturally compared to those produced using emerging agri-food technologies, (a finding that is in line with previous research, see for example Rozin et al., 2004 and Tenbült et al., 2005). However, even the acceptance of natural novel foods is low among the food allergic consumers. People's preferences for natural food appear outweigh their potential advantages for health. This may, of course, vary according to the extent to which the potential novel food delivers a benefit or a mitigation strategy which cannot be managed through application of alternative strategies, such as avoidance, and is a topic worthy of future research.

**Acknowledgements**

The authors would like to thank all respondents who filled in the questionnaires. This research has been done as part of a PhD project funded by the Allergy Consortium Wageningen, The Netherlands.

**Annex A: Selection Questionnaire for food allergic consumers**

1. Are you allergic to any food(s)?
    - ☐ No
    - ☐ Yes

2. For which food(s) are you allergic? (Multiple answers are allowed)
    - ☐ Peanut
    - ☐ Tree nuts
    - ☐ Milk
    - ☐ Egg
    - ☐ Wheat
    - ☐ Fruit
    - ☐ Vegetables
    - ☐ Soy
    - ☐ Sesame seed
    - ☐ Fish
    - ☐ Crustaceans
    - ☐ Celery
    - ☐ Other food(s), namely

3. Have you stopped eating/drinking this food(s)?
    - ☐ No
    - ☐ Yes

4. How long ago have you stopped eating/ drinking this food(s)?
    - ☐ 0 to 6 months ago
    - ☐ 6 to 12 months ago
    - ☐ 1 to 2 years ago
    - ☐ More than two years ago

5. Which symptoms occurred during the most severe allergic reaction ever? (Multiple answers allowed)

- Itching mouth
- Itching throut
- Itching ears
- Itching tongue
- Itchins lips
- Swelling of the tongue
- Swelling of the lips
- Running nose
- Stuffed up nose
- Sneezing
- Itching eyes
- Running eyes
- Red eyes
- Sweling of the throat
- Difficulty swallowing
- hoarseness
- Difficulty breathing
- stuffiness
- Wheezing
- Coughing
- Itching skin
- Redness of the skin
- Swelling of the skin
- Hives
- Increased eczema
- Nauseous
- Stomach cramps
- Vomiting
- Diarrhoea
- Dizziness
- Black out
- Faintness
- Lightheaded
- Feinting
- Other, namely……
- None of the above

**Annex B Information for food allergic consumers regarding food allergy and novel foods**

**If it happens to you: food allergy**

By Maartje van Eerd

Imagine kissing your boy friend and the next minute you are beeing wheeled off to a hospital because apperently you are alleric to peanuts. Every year this happens to some people. It also happened to Wendy (25) when she kissed her new boy friend. He had just eaten a portion sized bag with peanut M&Ms. Wendy is allergic to peanuts, which is a severe type of food allergy.

When someone is allergic to food, the body's immune system produces antibodies against proteins that are present in food, such as cow's milk, wheat, fruit, egg, fish, tree nuts and peanuts. Normally, the body does not produce antibodies against these proteins. Symptoms of a food allergy vary from eczema, stomach cramps, and swelling of the lips to more severe reactions such as an anaphylactic shock and sometimes even death. Approximately 8% of children and 2% of adults have one or more food allergies.
People with a food allergy have to avoid all foods that contain the proteins to which they are allergic because currently no cure exists. For Wendy this means avoiding all peanuts, which is difficult because peanuts are used as an ingredient for many different foods. 'In When I go out for my shopping, I have to check every product label to check the ingredient lists to make sure I do not accidentally eat something that contains peanuts,' explains Wendy. 'Even a product that is not supposed to contain peanuts, but which is produced in a factory that does process peanuts, can be dangerous for me.'
Wendy's parents noticed Wendy reacted badly to some foods when she was young, but did not know exactly what was wrong with her. When Wendy was four years old, she ate a peanut at a birthday. She had a bad reaction to the peanut and was rushed to the hospital. 'They performed various tests and I got diagnosed with peanut allergy,' says Wendy. From that moment on the foods which I could not, or could eat were at the centre of attention. My mother could no longer prepare the meals that she used to because she could not be certain that there were no traces of peanut. This had impact on our whole family. Nowadays, I prepare most meals myself because then I can be sure that there are no peanuts in it. Sometimes that is difficult because it prevents me from spontaneously going out to eat with friends. That is because everyone always has to take my peanut allergy into consideration. It is difficult because not everyone does that. 'Sometimes I go to birthday parties where peanuts are being served. This means that I

have to be extra carful to avoid getting in contact with the peanuts because I may get an allergic reaction from very small amounts of peanut. I always ask them to remove the peanuts. Many people will serve something else instead, but others cannot image that peanuts make me will, or that I may die from them'.

It can be very difficult to avoid peanuts. Her boy friend kissed her after eating peanut M&Ms. 'Obviously, he was terrified. He knew I am allergic, but had not realised that a kiss can be dangerous for me.' Everyone in her life becomes affected by my allergy. 'I can never just enjoy food,' Wendy explains, 'I always have to check the ingredients to see if the food is safe for me to eat, every day, every meal.'

**Novel food information for non-food allergic consumers, information scenario and for food allergic consumers**

It is possible to produce hypoallergenic foods. This means that these foods contain less of the substances that can cause an allergic reaction for people that are allergic for this substance. There are several ways in which foods can contain less allergens.

In this questionnaire we mention three different types of these novel foods:

- Natural novel foods: These are foods that are less allergenic because there are natural differences between different varieties of the same sort.
- Technological novel foods: these are foods that we know already but can be named novel, because a new processing technique or production method has been used, like extreme high pressure or high temperatures.
- Genetic modified novel foods: these are foods from which the allergens have been removed. Nothing has been added to these foods.

**Benefits of hypoallergenic foods**

The most important benefit of all these foods are that they do not cause allergic reactions, or maybe some mild complaints in the worst case. Because of this, allergic people do not have to be extremely alert to products to which they are allergic. This facilitates allergen avoidance.

They do not have to worry constantly that they might have a (deadly) allergic reaction when they eat something. Because of these novel foods, there will be more products for consumers to choose from.

Which methods are used to make foods hypoallergenic, does not matter. The benefits mentioned above can be reached by using natural novel products, but also by genetically modifying foods or by applying a new technological treatment, like a very high temperature or high pressure.

**Annex C: Neutral information for non-food allergic consumers**

**Food**

With “food” we mean all organic substances that are needed by a human being. With these substances, the body can produce energy to facilitate all processes in the cells. Which substances can or cannot serve the human being has been proved throughout the years through natural selection. Through trial and error is determined what is poisonous and therefore destructive is for the organism. This knowledge is transmitted in word or in writing.

Food for humans has been developed for a long time. First we ate our food mainly raw, but soon it became the habit to prepare our food. The food became more tasteful but also easier to digest. Our food has, from the fifties in the twentieth century, changed enormously. With the development and availability of food science, our food changed and improved. Conservation techniques make it possible to preserve food for a long time. In the sixties of the twenties century, a contra-movement arose, consisting of people that became vegan or vegetarian, and of people that started to make and sell biological food, that was grown in the ecological agriculture.

**Healthy food**

Every food consists of different nutrient in changing amounts. The highest change that the body receives enough of all nutrients is by eating varied food. The basic concept of healthy food that was recommended by the “Voedingscentrum”, makes sure enough nutrients are available for the body. These guidelines direct of a large amount of read, potatoes, rice, pasta, legumes, vegetables and fruits and two times a week fish. This is completed with dairy and meat, eggs or meat substitute and margarine or bake and frying products. Sufficient fluids are also essential.

Many people eat too much and in a wrong way. Healthy food contributes to a healthy life. It supplies nutrients that are necessary to keep the body healthy. Healthy food in combination with sufficient exercise is the base for a healthy weight and diminishes the risk on chronical diseases, like cardiac diseases, diabetic and several forms of cancer. Foods like sauces, snacks, cookies, candy and pastry are not included in a balanced diet. These products are providing too many calories. Furthermore they are less important in supplying nutrients. Healthy food also means: do not eat too much out side the balanced diet guidelines. Choose consciously for healthy food and enjoy it!

**Novel foods**

The last few years a lot of new foods have entered the supermarkets. In the questionnaire (of this research, which you will receive shortly) we will mention three types of novel foods.

- Natural novel foods: which are foods that are eaten around the world but are just recently introduced in the Dutch supermarkets.
- Technological novel foods: these are foods that we have known for some time, but can be named new, because a new processing technique or production method has been used, like extreme high pressure or high temperatures.
- Genetically modified novel foods: these are foods that have been improved by changing their genetic (or hereditary) characteristics.

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# Chapter 5

# Novel foods and allergy: regulations and risk-benefit assessment

Submitted for publication

**Abstract**

Hypoallergenic novel foods may have benefits for food allergic consumers. However, other novel foods may exacerbate the problems associated with food allergy. This chapter reviews the existing legislation associated with the introduction of novel foods and assesses the efficacy of such legislation with respect to allergy risks and benefits. Various regulations are in place to protect consumer health. These regulations require novel food safety to be assessed before they can enter the market, but do not specify how this assessment, which includes allergenicity should be performed. It is concluded that including a benefit assessment in the novel food legislation, may be beneficial.

## 5.1 Introduction

There has been considerable societal discussion regarding the potential advantages associated with the introduction of novel foods and ingredients into the food chain, in response to societal recognition of the potential benefits as associated with these products. Proposed benefits may relate to improvements in public health, diversification of nutritional intake, or improved food security or quality (Putten et al., 2006). The designation “novel foods” as used in the current discussion pertains to foods or food ingredients with no history of widespread and safe consumption. The novelty of a food can be the result of: (1) genetic modification (GM) of the food itself, or its production using genetically modified (GM) organisms, (2) the application of novel processing techniques, such as new types of heat processing, non-thermal preservation methods and the application of new processes catalysed by enzymes, or (3) the food in question having no prior history of consumption in general, or in a specific region or country, such as for “natural” non-GM foods (Putten et al., 2006). One rationale for developing novel foods is to reduce the incidence of food allergy by eliminating or substituting proteins which provoke allergic responses. However, it is important to note that other novel foods may exacerbate the prevalence of food allergy as novel potentially allergenic proteins are introduced into the food chain, or to the diets of individuals hitherto unexposed to them.

Food allergy, a hypersensitivity reaction initiated by immunologic mechanisms to normally harmless food components, affects between 5 to 8% of children and 1 to 2% of adults (Rona et al., 2007). In the discussion that follows, food allergy is understood to refer to IgE mediated reactions of the human immune system to food. The development of hypoallergenic novel foods and ingredients may be utilised to develop a food allergy management strategy that potentially improves the quality of life of food allergic consumers. However, it is also important to acknowledge that the introduction of novel foods and ingredients has the potential to introduce allergenic proteins into the food chain. For example, at the time of writing, concerns exist about the potential of novel foods to introduce new allergens into the foods chain (Putten et al., 2006). In addition, there is little information available regarding consumer attitudes independent towards novel hypoallergenic foods, independent of whether consumers suffer from a food allergy (Schenk et al., 2008). Thus, on one hand novel hypoallergenic foods may improve the quality of life of food allergic consumers by reducing dietary restrictions. On the other hand, novel foods have potential to exacerbate the incidence of food allergy. In both cases, it is important to examine how existing regulatory frameworks designed to optimise consumer protection deal with the case of novel foods and food allergy. For this

purpose it is interesting to compare these frameworks as being operational in different countries worldwide.

The aim of this chapter is to review the existing legislation associated with the introduction of different types of novel foods, to assess the efficacy of such legislation with respect to risks (and benefits) of novel foods associated with food allergy, and to identify where additional information may be required to protect food allergic consumers. The focus of the review will be the European legislation. This will be compared to a select number of legislations with well-established regulations pertaining to novel foods, i.e. Canada, the USA, and Australia-New Zealand. Existing regulatory frameworks have been developed to protect human health in relation to novel food safety. These frameworks do not indicate how novel food allergenicity should be assessed. Therefore, the safety assessment methods currently available for the different types of novel foods are presented. It is also important to note that many emerging food risk governance models posit that an assessment of both the risks as well as the benefits associated with a food issue are required, and furthermore, to broaden risk and benefit assessments towards the impacts on health and other socio-economic issues (Wentholt et al., in press). Therefore an overview of the potential benefits of novel foods for food allergic consumers will be discussed.

### 5.2 Novel food legislation

Various legislations have regulations in place that require novel foods be legally approved before entering the market. Such regulations usually also require that these novel foods be assessed for their safety. In an increasingly globalised and complex food system, it is important to consider how different legislatures consider specific food safety issues, as lack of regulatory harmonisation may be problematic if foods and food ingredients are exported between different regions of the world (Marvin et al., 2009)). This applies to novel foods and ingredients entering the food chain, whether as products which have the potential to sensitise new populations hitherto unexposed to the problematic proteins, or who may differentially respond to novel hypoallergenic foods assessed in different regulatory regimes.

#### 5.2.1 European Union

The EU defines novel foods as “foods and food ingredients that have not been used for human consumption to a significant degree within the Community” (European Commission, 2008a). To enable a novel food to be placed on the market in the European Union, Regulation (EC) 258/97 of the European Parliament and the Council applies

(European Parliament and European Parliament and the Council, 1997). At the time of writing, a new proposal for amendment of Regulation (EC) 258/97 is being discussed at the EU political level. As no decision has been taken yet to the adoption of the proposed amendments, it is not possible to discuss these[16]. When Regulation (EC) 258/97 went into force, it applied to novel foods and food ingredients that have not been available on the EU market to a significant degree before May 1997. The scope of Regulation (EC) 258/97 initially also included GM foods and ingredients. However, since 2005, GM foods and ingredients have to be assessed for their safety, and to be approved for their market introduction under Regulation (EC) 1829/2003 (European Parliament and the Council, 2003b).

Before being placed on the EU market, the novel foods and food ingredients referred to in Regulation (EC) 258/97 must undergo a safety assessment, as a result of which an authorisation decision may be taken by the European Commission. This safety assessment focuses on the systematic and objective evaluation of all available information about the novel food. During the assessment procedure, the competent authority of a Member State that receives an application must make an initial assessment and determine whether or not an additional assessment is required. If neither the Commission, nor the Member State raises an objection, and if no additional assessment is required, the Member State informs the applicant that he may place the product on the market. In other cases, a procedure is followed in which the European Commission seeks scientific advice from the European Food Safety Authority, (EFSA) based upon which the European Commission drafts a decision. This draft decision is subsequently submitted to the Standing Committee on the Food Chain and Animal Health, and, depending on the outcomes of that, may be submitted to the Council of Ministers, before an official decision can be taken by the Commission (SCADPlus, 2008).

The information needed when a novel food application is made, depends on the characterisations of the type of novel food, and is described in Commission recommendation 97/618/EC (European Parliament and European Parliament and the Council, 1997). Specifically, information is required in thirteen categories, ranging from a specification of the novel foods and the effect of the production process on the novel foods to projections of anticipated intakes, which are needed to evaluate the dietary and nutritional consequences of the novel food. Toxicological information, which includes

[16] The proposal for amendment of Regulation 258/97 intents to exclude foods derived from cloned animals and their offspring from the scope of the regulation, as well as to have foods produced by nanotechnology to undergo a specific risk assessment before being approved for use.

Table 5.1 Evaluated novel foods in the EU (EC, 2008a)

| Description of Food or Food Ingredient | European Commission decision | Additional information |
|---|---|---|
| Stevia rebaudiana (plant and dried leaves) | Refused | Sweetener |
| Phospholipids from egg yolk | Authorised | Novel processing technique |
| Yellow fat spreads with added phytosterol-esters | Authorised | Lower blood cholesterol |
| Fruit preparations pasteurised using a high pressure treatment process | Authorised | Novel processing technique |
| Nangai nut | Refused | novel food |
| Bacterial dextran | Authorised | Polysaccharide for use in bakery products |
| Salatrim | Authorised | Fat replacer |
| Tahitian Noni Juice | Authorised | Ingredient in fruit juice mixtures |
| Trehalose | Authorised | Sweetener |
| REDUCOL™ | Authorised | Lowers blood cholesterol |
| Plant sterol enriched bakery products, grain based snack products and gum Arabic pastills | Authorised | Improves blood cholesterol |
| Coagulated potato protein and hydrolysates thereof | Authorised | Novel food ingredient |
| DHA-rich Oil | Authorised | Novel food ingredient with energy reduction effect |
| Phytosterol enriched fat ingredient – Diminicol | Authorised | Lower blood cholesterol |
| Multibene® - Ingredient | Authorised | Lower blood cholesterol |
| Plant Sterols and Sterol Esters | Authorised | Lower blood cholesterol |
| Rapeseed oil high in unsaponifiable matter | Authorised | Novel food ingredient |
| Maize germ oil high in unsaponifiable matter | Authorised | Novel food ingredient |
| ENOVA™-oil Diacylglycerol Oil (DAG oil) | Authorised | Replace conventional oils |
| Phytosterol-esters: Use in a range of products | Authorised | Lower blood cholesterol |
| Iodine enriched wild-type eggs | Refused | Novel food (consumption egg) |
| Betaine | Refused | Use in drinks, cereal products, confectionary and dairy products |
| Deer horn powder | Refused | Dietary supplement |
| Isomaltulose | Authorised | Sweetener |
| Lycopene from Blakeslea trispora | Authorised | novel food ingredient |
| Allanblackia seed oil for use in yellow fat spread and cream based spreads | Authorised | Ingredient in yellow fat and cream based spreads |
| α-Cyclodextrin | Authorised | Added as dietary fiber |
| Diminicol® rice drink with added phytosterols | Authorised | Extended use of phytosterol ingredient diminicol |
| Tagatose | Authorised | Sweetener |
| MultOils (oil containing a diacylglycerol-rich fat component and a free phytosterol esters component) | Authorised | Lower blood cholesterol |
| Baobab (Adansonia digitata) dried fruit pulp | Authorised | Use in fruit bars and smoothies |
| Refined Echium oil (Echium plantagineum) | Authorised | Novel food ingredient |

information about the potential allergenicity, is also required (European Parliament and the Council, 1997). These recommendations only indicate what type of information should be presented. It does not recommend how this information should be gathered.

This may relate to the fact that allergenicity assessments need to be carried out on a case-by-case basis (Taylor and Hefle, 2001).

At the time of writing, a total of 91 novel foods have been submitted for authorisation in the EU (European Commission, 2008b). Table 5.1 gives an overview of novel foods that have received an EU decision about their authorisation under Regulation (EC) 258/97 (European Commission, 2008a). GM novel foods that are only novel because of genetic modification are not listed in this table. This is because not all GM novel foods which have been authorised in the EU have been evaluated under Regulation (EC) 258/97. Some of the applications have been withdrawn, and for others the assessment procedure is still pending at time of writing. Most novel food applications that have been made in the EU are products that can be used as an ingredient for food products. The European Commission has made a decision on 37 novel foods. Five of these novel foods have been refused because their compliance with the criteria laid down in article 3 (1) of Regulation (EC) 258/97 could not be demonstrated. This article states that "novel foods and food ingredients must not present a danger to the consumer; mislead the consumer or differ from foods or food ingredients which they are intended to replace to such an extent that their normal consumption would be nutritionally disadvantageous for the consumer". In the case of Stevia rebaudiana, a novel food to be used as a sweetener (SCF, 1999) and of nangai nuts, a novel introduction to the European market from the pacific region (SCF, 2000), the scientific opinions were based on the lack of essential data, including, but not confined to, data on allergenicity, pre-empting a conclusion on the safety of these products. For betaine, a food additive claimed to prevent cardiovascular disease, the scientific opinion is explicit about the fact that no clarification has been provided for test-substance related effects in an animal toxicity study, and therefore no safe levels could be established (EFSA, 2008). For iodine-enriched eggs, which result from the combination of the Columbus egg, rich in polyunsaturated fats, and the Japanese Hikari egg, which is rich in Iodine, the authorities of the EU member state (Belgium) where the application had been filed raised objections based on the possibility of the exceedance of the safe upper level of iodine intake by consumers, about which the other members did not express disagreement. Thirty-two novel foods have been authorised for marketing in the EU because their safety has been sufficiently demonstrated and because they do meet the criteria as laid out in Regulation (EC) 258/97. The European Commission's Community Register of GM organisms with authorised uses in food and feed currently contains 26 GMOs, including six GM cotton, 12 GM maize, biomasses from two GM micro-organisms, three GM oilseed rape, two GM soybeans and one GM sugar beet. These have several authorised uses each, for

example the BT11 maize that is authorised to be used for foods and food ingredients, food additives, feed, and for other products (European Commission, 2008c). The dossiers on the novel foods as summarised in the published safety assessments do contain information in the relevant categories from Commission recommendation 97/618/EC. However, little information can be found on the allergenicity assessment of the non-GM novel foods in the published approvals and summaries of the dossier evaluations, given that the original dossiers are usually confidential and not freely accessible. This contrasts with the evaluations of GM foods, for which the allergenicity assessment is a common feature. In the summaries of the evaluations of most non-GM novel foods dossiers, allergenicity assessment is not mentioned at all and in the summaries of dossiers where attention is paid to the potential allergenicity of the novel food, the assessment is limited to remarks that there is no reason for concern, or that there are no indications of allergenicity. How this conclusion was reached is not specified, however. For only a few novel foods such as Ice Structuring Protein, which has benefits both in terms of nutritional and organoleptic profile, and greater temperature stability (Crevel et al., 2007) the scientific opinion's summary of the dossier provides more information about the allergenicity assessment such as amino acid sequence comparison to known allergens, *in vitro* breakdown by pepsin, IgE binding screening, and skin prick tests (CBG-MEB, 2008). For some novel foods, scientific studies can be found that investigate the (potential) allergenicity. Crevel et al. (2007) report a study with human subjects who consumed ice structuring protein for several weeks and remained in good health, and who developed no IgE antibodies, affirming previous conclusions that these ice structuring proteins are unlikely to have allergenic potential (Crevel et al., 2007). In addition, the EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA Panel) describes a sensitisation study in guinea pigs, which received repeated subcutaneous injections (i.e. beneath their skin) of extracts of leaves of the noni plant (*Morinda citrifolia*), which can be used as an ingredient for fruit juices, but which did not exhibit signs of allergic reactions after oral challenge with the same extracts (EFSA, 2008). This is similar to a sensitisation test in guinea pigs that has been performed with the juice of noni fruits (SCF, 2002). Some of the opinions on these applications also mention potential health benefits. An example is provided by phytosterols, which potentially inhibit the absorption of cholesterol (CBG-MEB, 2008). On the other hand, the assessment of chia seeds, rich in omega-3 fatty acids and a potential source of antioxidants, as a novel food by EFSA's NDA Panel revealed cross-reactivity with peanut in serum binding and with sesame in skin prick testing when chia was tested (EFSA, 2008).

In addition to legislation regarding the marketing of novel foods, the EU also has legislation regarding the labelling of allergens. Novel foods are subjected to the general labelling requirements (Directive 2000/13/EC), but they may require specific additional information. Directive 2003/89/EC amends the general labelling directive and states that in order to protect food allergic consumers, the use of certain ingredients should be specified on the product label. These ingredients are cereals containing gluten, crustaceans, eggs, fish, peanuts, soybeans, milk and dairy products, nuts, sesame seeds, and sulphite at concentrations of at least 10 mg/ (European Parliament and the Council, 2003a). It should be noted that this labelling directive applies to foods that are available in the EU. This directive will only apply to novel foods, once they have been approved in the EU under regulation 258/97.

### 5.2.2 Australia- New Zealand, Canada and USA: differences and similarities with EU legislation

Figure 5.1 gives an overview of the novel foods safety assessment procedures in the EU, in comparison to procedures in Canada, Australia-New Zealand, and the USA.

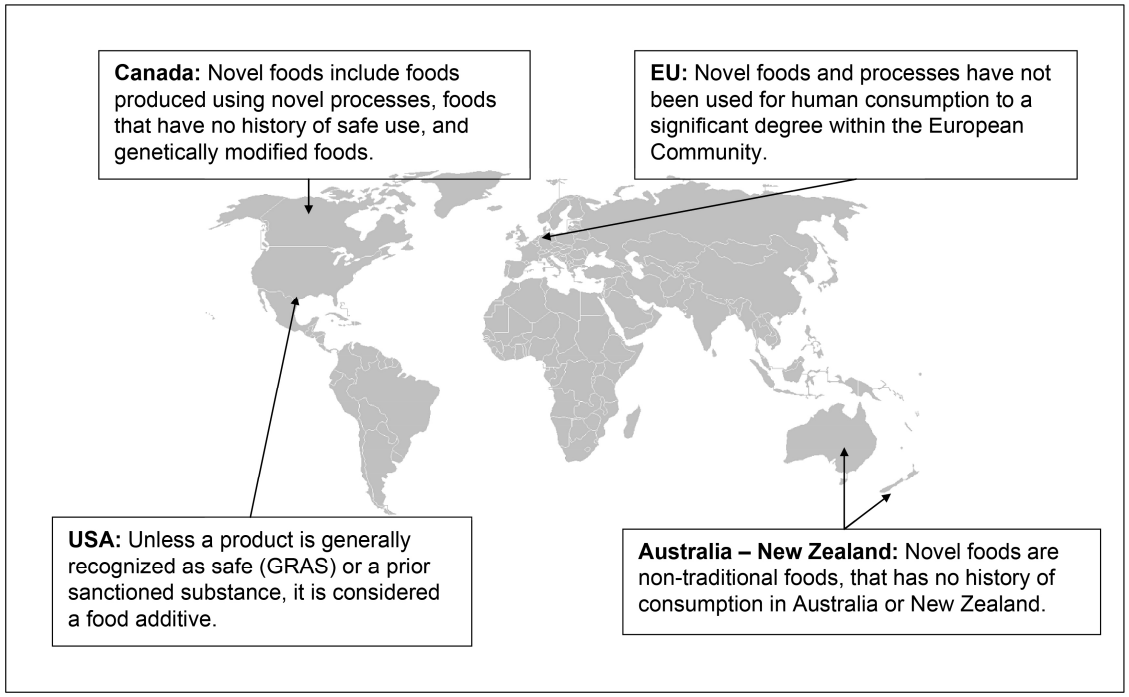


Figure 5.1 Legal categories of novel foods and processes in the food legislations of EU, Canada, Australia-New Zealand and USA.

The Canadian legislation describes novel foods as foods that result from a process not previously used for food, as products that do not have a history of safe use as a food, or as foods that have been modified by genetic modification also known as genetically modified foods, GM foods, genetically engineered foods, or biotechnology derived foods (Health Canada, 2008a). In practice, this means that most of the novel foods assessed are GM or derived from certain mutation-bred crops. The Canadian approvals also pertain to a number of novel processes, e.g. UV-disinfection of apple juice and high-pressure pasteurisation of meat (Health Canada, 2008b). Allergenicity assessment is included as part of the approval process. How the potential allergenicity should be assessed is specified in neither Canadian legislation nor European legislation.

The Food Standards Australia New Zealand (FSANZ) agency describes novel foods as non- traditional foods with characteristics that require an assessment of public health and safety considerations (Food Standards Australia New Zealand, 2008b). A non-traditional food is a food that has no history of human consumption in Australia or New Zealand. This also includes substances derived from a food, that have not been consumed other than as a component of the food, and substances that come from a source without history of consumption in Australia or New Zealand. Key areas influencing the interpretation of the term 'history of human consumption' are the length of use; the extent of use; the quantity (level of intake) of use; and the purpose or context of use (Food Standards Australia New Zealand, 2008a). As is the case in Canada and the EU, allergenicity assessment is included as part of the approval process, but regulations neither specify how this allergenicity assessment should be performed. The USA does not specifically distinguish novel foods as a class of products. Instead, a substance that will be added to food is subject to premarket approval by FDA unless its use is generally recognized as safe (GRAS) by qualified experts, or if it is a prior sanctioned substance that the FDA or USDA determined safe for use in food before 1958 (International Food Information Council US Food and Drug Administration, 2008). The GRAS procedure is a notification procedure. A product is GRAS through (1) scientific procedures, which may be corroborated by unpublished studies and other data and information, or (2) experience based on common use in foods requires a substantial history of consumption for food use by a significant number of consumers (International Food Information Council US Food and Drug Administration, 2008). If a substance is not generally recognised as safe or a prior sanctioned substance, it is considered a food additive and must be subject to a mandatory safety assessment by FDA, which includes comprehensive toxicological testing, genetic toxicity, acute oral toxicity, short term toxicity, (sub)chronic toxicity, and reproduction and developmental toxicity (International

Food Information Council US Food and Drug Administration, 2007). Potential allergenicity is not specifically mentioned in the FDA Redbook, which applies to all food additives. The potential allergenicity of transgenic proteins has been considered in their safety assessment (International Food Information Council US Food and Drug Administration, 2008). It should be noted that the definition of a food additive may diverge between the American and other legislations. In the EU, for example, food additives are defined by Directive 89/107/EEC as food substances that are added to foods in limited quantities and that serve a technological purpose, examples being colorants and sweeteners. As for the other legislative frameworks considered, allergenicity assessment is included as part of the approval process, but how this should be done is not specified.

When comparing the various novel food regulations, it is relevant to note that that Canada regulates GM foods as novel foods, where in the EU this has not been the case since 2005 with the implementation of a specific regulation pertaining to GM food and feed, i.e. 1829/2003, amending the Novel Food Regulation (EC) 258/97 (European Parliament and the Council, 2003b). The Food Standard Australia New-Zealand (FSANZ), as is the case in the EU, does not classify GM foods as novel foods. Canadian legislation refers to a lack of a history of *safe* use of the food for the food to be novel, whereas EU legislation only refers to a history of use. The FSANZ does not use 'history of safe use' as a criterion to define a novel food. Instead, the FSANZ only refers to a 'history of use' in Australia of New Zealand when describing non traditional foods. Appropriate regulatory agencies in each country assess the safety of all novel foods proposed for sale in the particular countries. When comparing the safety assessment procedures, caution must be taken because definitions of novel foods in these countries differ and, as a consequence, the assessment procedures also differ, in such a way that they cannot be compared directly. All countries do include allergenicity in the safety assessment. However, no comparisons are possible since the allergenicity assessment procedures are not described. It is important to note that although the various novel food legislations have some similarities, authorisation of a novel food in one country does not imply that the novel food can be imported to another country without further safety assessment.

### 5.3 Novel Food safety assessment

Before the safety of novel foods can be discussed, two points need to be clarified. The first point is that sensitisation to potential allergens is required before allergenic reactions will take place upon re-exposure to these same allergens. Food products that contain potentially sensitising novel proteins could change the exposure of the

population to these proteins, thereby potentially giving rise to the development of new allergies. For the allergenicity assessment two aspects are important: (1) *de-novo* sensitisation by completely new allergens and (2) cross-reactivity with allergens that are similar to the ones to which the food allergic consumer is already sensitised. *De-novo* sensitisation by completely new allergens is more difficult to predict than cross-reactivity. Therefore, this chapter focuses on potential cross-reactions of novel foods rather than on sensitisation. Given that, by definition, novel foods have no history of safe use in the EU, safety assessment is necessary to assure human health. The second point is that where possible, safety assessment of foods uses traditional foods and ingredients as reference points and the assessment process focuses on the differences between these and the novel foods and ingredients under assessment (Howlett et al., 2003). An example of this is the evaluation of substantial equivalence of oil derived from two distinct GM cotton lines, Insect Protected line 531 and Roundup Ready line 1445. It was agreed that processed oils derived from these lines were equivalent, in composition, to oils from conventional cottonseed varieties (ACNFP, 2008).

The methods available to test novel foods allergenicity vary for and depend on the type of novel food under assessment. Table 2 provides an overview of the various (complementary) assessment methods that are available to assess the safety of the different types of novel foods. This Discussion of the available methods to assess allergenicity of GM novel foods for which the available methods are documented is provided (Codex Alimentarius Commission, 2002; FAO/WHO, 2001). This is followed by a discussion of possible methods to determine allergenicity of non-GM technological novel foods, for which at the moment fewer methods are available. This paragraph ends with a discussion of available allergy testing methods for the other novel foods.

Table 5.2 Assessment strategies available for different types of novel foods.

| | GM | Non GM tech | Non Native |
|---|---|---|---|
| Source/ Phylogenetic relationship | ● | | ● |
| Amino acid sequence | ● | | |
| Pepsin resistance | ● | ● | ● |
| IgE binding | ● | ● | ● |
| Level of expression novel protein | ● | | |
| Animal models (when available and validated) | ● | ● | ● |
| Previous human exposure (to novel food) | | | ● |

### 5.3.1 Safety of GM novel foods

The allergenicity assessment of GM products, (usually common food crops into which a foreign gene coding for a novel protein has been introduced) considers both the novel protein and the product that receives the novel protein. A specific concern for food safety in the case of GM novel foods is the expression of novel allergenic proteins in transgenic crops. No single test exists that is fully predictive of the potential allergenicity of any specific novel protein (Taylor, 2006) and therefore the assessment of potential allergenicity should combine various criteria, according to the "weight of evidence approach" recommended by Codex Alimentarius, including the source of the protein, amino acid sequence homology to known allergens, pepsin resistance and specific serum screening (Codex Alimentarius Commission, 2002).

One of the criteria considered in the assessment of potential allergenicity of GM novel foods is the gene source. If, for example, the gene has been obtained from an allergenic source, i.e. an organism known to cause allergic reactions in allergic consumers, then the potential allergenicity of the gene product in these consumers has to be considered. Moreover, if the protein encoded by the specific gene, i.e. the gene product has already been established as an allergen, then it has to be verified whether it has maintained its allergenic properties in the transgenic plant (Stewart et al., 2000). An example of the product of a gene derived from an allergenic source is the Brazil nut's 2S albumin, an allergenic protein that showed reactivity in Brazil nut allergic consumers after its transfer to an experimental GM soybean (Nordlee, 1996). If the gene source has an unknown history of allergenicity this still requires further investigation on whether it may be allergenic in a transgenic plant according to various criteria described below. In addition, also the history of allergenicity of the recipient organism of genetic modification is considered with regard to potential changes in intrinsic allergens caused by the genetic modification.

Amino acid sequence comparison may be a tool to estimate whether a novel protein has allergenic potential. IgE cross-reactivity between the novel protein and a known allergen should be considered a possibility if there is more than 35% identity in a segment of 80 or more amino acids, or if both proteins share a segment of identical contiguous amino acids (Codex Alimentarius Commission, 2002; FAO/WHO, 2001). If there is no sequence homology, this indicates that the novel protein is not similar to known allergens and less likely to be cross-reactive to known allergens. A positive sequence homology result indicates that the protein is potentially cross-reactive with the known allergens. If the novel protein's similarity to allergens is considered further, it

should be assessed using serum from individuals sensitised to the identified allergenic source (Codex Alimentarius Commission, 2002). Orruño and Morgan (2006) note that sequence homology and structural similarity to known allergens are not sufficient to predict cross-reactivity involving conformational epitopes consisting of a discontinuous amino acid sequence along a folded protein (Orruño and Morgan, 2006). According to these authors, more information is needed to exactly pinpoint epitopes. They do not explain their assumption as to why it is not possible to predict potential cross-reactivity of conformational epitopes. However, Aalberse and Stadler (2006) claim that allergenic potential can be easily assessed by a combination of *in silico* homology searches with a 50% cut-off in overall sequence alignment, and *in vitro* IgE antibody assays (Aalberse and Stadler, 2006). They claim that the major limitation of bioinformatics, i.e. the use of computer algorithms to investigate data on and predict the properties of biological molecules, is the number of allergens missing from the database, particularly minor allergens from airborne sources, such as pollen, insects and moulds. Aalberse and Stadler (2006) do acknowledge that by focussing on the primary sequence, post-translational modification, which is a possible source of cross-reactivity is overlooked since these processes are not fully determined by only the DNA sequence.

Since a number of food allergens are stable to digestion, the latter represents an important criterion to predict allergenicity. While not all stable proteins are allergens, for the purpose of allergenicity evaluation, digestible proteins are believed to have lower potential for systemic exposure of the intact protein (Taylor, 2006). This means that such proteins are less likely to sensitise and cross-react through the oral route and trigger allergic reactions upon subsequent oral exposure. Resistance to degradation by the stomach enzyme pepsin in *in-vitro* model tests indicates that further analysis should be conducted. A lack of resistance to pepsin *per se* does not exclude that the novel protein can be an allergen (WHO, 2003).

For proteins that originate from a known allergenic source or that have sequence homology with a known allergen, testing in immunological assays should be performed where sera are available. If a novel protein from a known allergenic source has negative results in *in vitro* immunoassays, this protein should undergo additional testing such as skin prick tests. A positive result would indicate a potential allergen. For proteins from sources not known to be allergenic and which do not exhibit sequence homology to known allergens, targeted serum screening with sera from patients allergic to allergens that are broadly related to the source of the transgene may be considered (WHO, 2003).

Very little information exists regarding threshold doses for sensitisation and cross-reactions. According to Taylor (2006), however, the level of expression of the novel protein is another factor that should be considered in the safety assessment of GM novel

foods. Foods produced through GM are less likely to become allergenic if the novel proteins are present in low concentrations, especially with regard to the expression in the edible portion of the modified plant.

It should be noted that the allergenicity assessment strategy for transgenic proteins cannot be applied to novel foods in which a gene has been down regulated, thereby preventing the presence of a potential allergen in the product. When such a hypoallergenic novel food is developed, the safety assessment should involve the same testing procedures, and in addition the reduced allergy impact of this allergen should be assessed.

### 5.3.2 Safety of non-GM technological novel foods

During food processing, allergenicity can be altered by various procedures such as storage time, preparation techniques, heating, prolonged washing and interactions with other food components. As a result, the allergenic potential may be unaffected, decreased or even increased. Alterations in stability caused by processing may alter the resistance to digestion and the nature of the interaction with the immune system. Allergenicity can also be increased when new epitopes are exposed at the surface of the protein or formed by chemical reactions such as the Maillard reaction between carbohydrates and proteins while it can be reduced when former conformational epitopes are lost. An example of the exposure of a new epitope is the protein Beta-lactoglobulin from cow milk, which has a linear epitope buried within its structure. This linear epitope becomes exposed when the proteins structure changes through denaturation (Liu et al., 2007). Alterations in allergenicity due to the exposure of new epitopes cannot be detected using amino acid sequence comparisons, which is an important assessment step for GM novel foods. For GM novel foods the novel protein was the most important subject of assessment. The proteins in the product are not known for all non-GM technological novel foods, which makes this strategy less useful.

Validated animal models may offer the most direct approach for the determination of the intrinsic sensitising potential of novel proteins in the future. Currently, however, no validated and widely accepted animal model is available (Orruño and Morgan, 2006). Food allergy follows exposure to food as it is normally eaten, and not following exposure to isolated proteins. It is important to note that the normal allergenicity of the protein may be influenced by the interaction with other components present in the food matrix, such as lipids and sugars and of wider aspects of structure and localisation (Orruño and Morgan, 2006).

For GM novel foods, the result of the safety assessment procedure is a conclusion as to the likelihood of the novel protein being an allergen. Since for the assessment of non-GM technological novel foods, less well described assessment methods are available, the outcome of this safety assessment contains more uncertainties.

### 5.3.3 Safety of natural novel foods

Kiwi is an example of a food that had an unknown history of allergenicity, but nonetheless manifested itself as allergenic (Lucas et al., 2005). In the case of kiwi, two issues are at stake, including cross-reactivity between the kiwi and known allergens, such as bananas and latex, and de-novo sensitisation for the kiwi itself. Whilst the cross-reactivity of new proteins is assessed for GM foods following a weight of evidence approach, this approach will not always be feasible for each new protein within a novel food, such as kiwi. If a food is completely new and it is not feasible to follow a weight of evidence approach for all new proteins within a novel food, the currently available allergenicity tests will not be sufficient to identify a truly novel allergen (Dearman and Kimber, 2009). Animal models could provide insight in the potential allergenicity of the food. Although currently no validated and widely accepted animal model is available, this is the most direct approach for determining the intrinsic sensitising potential of novel foods (Orruño and Morgan, 2006).

Gubesch et al (2008) designed an approach to screen novel foods for the presence of pan-allergens, IgE binding of food allergens and clinical relevance of IgE binding. Their conclusion is that this three-step approach seems to be applicable for allergenicity testing of natural novel foods (Gubesch et al., 2007). However, they do recognise that as long as no validated methods for assessing *de novo* sensitisation capacity are available the overall allergenic potential of novel foods is impossible to predict. If indications for cross-reactivity exist based on the allergenic history of the food or its phylogenetic relationship with other allergenic foods, it is recommended that the allergenicity assessment of foods and food proteins should include immunoglobulin E (IgE) from the sera of allergic patients using tests such as solid phase immunoassays (RAST, ELISA, EAST). When the identification of the allergenic components of a food material is required, SDS-Page followed by immunoblotting is generally applied.

### 5.3.4 Novel food safety

The end result of the assessment procedures is a conclusion as to the likelihood of the novel foods being an allergen. Depending on the type of novel food, and the

available information about that novel food, the likelihood contains varying uncertainty. No safety or risk assessment procedure can lead to the guaranteed safety of novel foods for food allergic consumers, as the allergenicity of any given food or protein cannot be precluded completely, although the list of major food allergens is relatively limited (Breiteneder and Mills, 2005). For food allergic consumers who need to avoid all foods that contain the protein(s) to which they are allergic, this likelihood information is not sufficient (Putten et al., in press). Research about the labelling needs of food allergic consumers (Cornelisse-Vermaat et al., 2008b) shows that one of the problems faced by food allergic consumers is the uncertainty about whether a product contains allergens or not, especially when “may contain” labelling is used. Some food allergic consumers may even ignore the warnings on the label and try the food product to test whether an allergic reaction will occur and if it does never buy the product again (unpublished data). This phenomenon may not always be noticed by post-market monitoring. Consumers may respond similarly when informed about the remaining uncertainties of the current allergenicity assessment procedures. This calls for complete, clear and publicly available allergenicity risk assessment information that allows consumers to interpret the risk assessment results and make the risk management decisions that meet their individual needs best. Health professionals and patient organisations may play an important role in interpreting the allergenicity risk assessment information and helping food allergic consumers to decide whether a novel food is safe for them. Another factor adding to the uncertainty associated with the results of the safety assessment procedures are individual (genetic) differences in allergic responses. It has been frequently observed that different individuals react differently to different proteins within the same allergenic food (Orruño and Morgan, 2006). So-called major allergens provoke an allergic reaction in more than 50 percent of the patient population. In addition, minor allergens exist to which less of the population is allergic. When a major allergen is removed or mutated, some patients still may react to the minor allergens in a product, which makes it not safe for them to consume at all.

The questions that remain relate to the level of risk which is acceptable, i.e. which level of safety is safe enough for food allergic consumers. The safety of a specific novel food depends on the allergy of an individual. Deciding when a food is safe for enough people, so it can be allowed on the market is a task for risk managers. The information that a safety assessment procedure provides is a first requirement to make further evaluations about whether novel foods may improve quality of life of food allergic consumers.

### 5.4 Potential benefits of novel foods for food allergic consumers

Various novel food regulations aim to ensure consumer protection and require therefore risk assessment before novel foods can be marketed. At the present time, food risk management decisions are primarily based on risk assessment information, and allergy assessment does not differ in this regard (FAO/WHO 1998). Emerging food risk governance models are based on an assessment of both risks and benefits associated with a food issue, and, furthermore, that these risks and benefit assessment should be broadened to embrace not only health impact, but also other socio-economic and ethical impacts (Wentholt et al., in press). In the case of novel foods there are arguments to support the idea that this broader definition of impact assessment should be formally included in management decisions. Formal inclusion at the assessment stage would imply the introduction of novel methodological approaches to metricisation of risk and benefit so that both can formally be considered at the management stage.

Food allergic consumers may profit from benefits of hypoallergenic novel foods through increased dietary variation and reduced restrictions on product selection and thereby reduction in the social limitations that food allergic consumers experience. Food allergy can have a profound impact on quality of life, not only because of the immediate clinical effects related to individual's allergic condition, but also because of the alterations in daily life that have to be made to prevent the occurrence of symptoms and the influence on psychosocial functioning of the individual (Blok et al., 2007; Oude Elberink et al., 2002; Sicherer et al., 2001). Exposure to a food allergen can result in anaphylaxis, which may be severe enough to be life-threatening (Jackson, 2003; Sampson, 1999a). Other factors potentially influencing the quality of life of food allergic consumers include increased time spent shopping (Cornelisse-Vermaat et al., 2008b; Voordouw et al., 2009) and increased costs to both the household and to the health services (Fox et al., accepted, subject to revision).

Thus novel hypoallergenic novel foods have the potential to improve the quality of life of food allergic consumers, although one might assume the impact on quality of life experienced by the allergic consumer is contingent on the degree of severity of the reaction experienced and the level of certainty that it will be avoided by consuming the hypoallergenic novel food. Against this, there is also potential for novel foods to increase the prevalence of allergic responses, through the introduction of problematic proteins into the food chain. When novel foods are considered to be safe for food allergic consumers, this can become a benefit. However, the results of the safety assessment procedures regarding allergenicity are conclusions as to the likelihood of the novel foods being an allergen. This means that the conclusions regarding benefits are somewhat uncertain.

Another issue is that allergenicity is not a simple matter of deciding whether a novel food is allergenic. Depending on the allergenic content and the individual response of the food allergic consumer, one novel food may be more allergenic than another. The same principle applies to benefits. When a novel food is considered to be hypoallergenic, it means that it contains less allergen than the traditional variant of the food. A question arises as to what level of certainty regarding the hypoallergenicity of novel foods is required for novel foods to be used as allergy management strategy. No legal definition of hypoallergenic exists, although in clinical terms hypoallergenic formulas (infant milk) are defined as those that are tolerated by ≥90% of infants with documented cow's milk allergy (Herz, 2008). In an ideal situation absolute certainty regarding the absence of potential for allergic reactions would be available. For most novel foods, this absolute certainty cannot be provided. Absolute certainty about the hypoallergenicity of the novel food or ingredient may not be required by all consumers. However, it is important to make information about the risk and benefit assessment available to food allergic consumers, allowing them to make their own risk management decision. How this information should be made available to consumers needs to be addressed in future research. Formal risk assessment procedures should also consider potential benefits. Regulations should take this into account as well and make the results of the risks (and benefit) assessments of novel foods publicly available.

Currently, the risk assessment procedures do not include the potential severity of the allergic responses. This information is relevant for risk managers, especially when considering the potential benefits of novel foods. Foods that are not allergenic may have more benefits for people with a severe and life-threatening allergy than for people with a mild allergy, since the former are likely to experience more problems with the strict and necessary food avoidance. However, the increased severity of an allergic response may also be associated with an increased level of uncertainty regarding the hypoallergenic properties of the food or food ingredient (Voordouw et al., 2009). Including the potential severity of an allergic reaction to a novel food will probably entail clinical testing which may have its ethical and practical limitations.

No summary of novel food applications in the European Union mentions benefits of the novel food regarding hypoallergenicity. It can be envisaged though that some of the experiments that may be carried out *in-vitro* or *in-vivo* with human or animal subjects to support health-claims can also provide additional, useful indications of any safety issues linked to the consumption of the novel food. It should be noted that such health claims are not assessed under regulation 258/97, but have to be assessed through a separate procedure, which falls outside the scope of this review. However, at the time of writing, no novel foods that have been legally authorised by the European Union could

be identified as hypo-allergenic. However, among the novel foods that have been assessed in Canada are “delicious soybean” and “TUSC-1 wheat”, in which the levels of major allergenic proteins in have been reduced. However, the reported purpose of these modifications relate to organoleptic or technical properties. In addition to this, it might be possible that new hypoallergenic foods with benefits for food allergic consumers exist that are not listed as novel. Apparently, current authorisation applications within the EU have not been primarily developed for their reduced allergenicity. However, it is possible that new food products access the EU market without evaluation under Regulation (EC) 258/97 because they are not considered novel according to EU directive 258/97. An example is the Santana apple, an apple cultivar that is the result from the crossing of the cultivars Elstar and Priscilla. The aim of this crossing was to combine the fruit quality of Elstar apples with the disease resistance of Priscilla (Maas and Berker, 2008). There is evidence that Santana apples are hypoallergenic, at least for some consumers (Kootstra et al., 2007). Other examples can be found in literature such as rice (Nakamura and Matsuda, 1996), soybean (Herman et al., 2003), apple (Gilissen et al., 2005), and peanuts (Dodo et al., 2005). However, this review was limited to novel foods and a review of other new foods is recommended for the future. It may be worthwhile to investigate how many other unusual but not novel foods exist that may be associated with hypoallergenic properties.

### 5.5 Conclusions

This chapter reviewed allergenicity legislation, assessment procedures, and potential benefits of novel foods to improve quality of life of food allergic consumers. Various regulations are in place to protect consumer health. These regulations require novel food safety to be assessed before they can enter the market. However, the current regulatory frameworks do not specify how these assessments should be performed. The EU recommends which information is needed for a novel food application, but besides from mentioning that allergenicity information is required, it is not specified how this allergenicity assessment should be performed. In Canada, the USA and Australia/ New Zealand allergenicity assessment is also part of the approval procedure, but how this assessment should be performed is not specified in the legislations. The may relate to the fact that the safety assessment methods available and best suited depend on the type of novel food under assessment. None of the safety assessment include benefits assessment. However, when a hypoallergenic novel food with benefits for food allergic consumers is being evaluated, it can be argued that information about the potential

benefits should be formally included in management decisions and therefore the assessment of benefits would be helpful.

The end result of the assessment procedures is a conclusion as to the likelihood of the novel food having allergenic potential. This implies that for approved novel foods, some uncertainty remains regarding the allergenicity. How consumers respond to this uncertainty needs to be addressed in future research.

# Chapter 6

# General discussion

Food allergy is defined as a hypersensitivity reaction that involves the immune system (Patriarca et al., 2009). Food allergy affects 5-8% of children and 1-2% of adults, although about 20% of people report an adverse reaction to food, which makes it an important health issue (Rona et al., 2007). At the time of writing, the only reliable treatment of food allergy is strict avoidance of the problematic foods. Food allergy can have a profound impact on quality of life, not only because of the immediate clinical effects related to an individual's allergic condition, but also because of the alterations in daily life that have to be made to prevent the occurrence of symptoms and the influence on psychosocial functioning of the individual (Blok et al., 2007; Oude Elberink et al., 2002; Primeau et al., 2000; Sicherer et al., 2001).

Hypoallergenic novel foods are of interest to the management of food allergies. Food allergic consumers may profit from the availability of hypoallergenic novel foods, and possibly also consumers who have an increased risks of developing food allergies. Besides the potential benefits of hypoallergenic novel foods, other novel foods may increase food allergy prevalence.

The research presented in this thesis investigated whether novel foods can be used as part of an allergy management strategy. Before novel foods can be successfully used for this purpose, food allergic consumers need to accept these hypoallergenic novel foods. In addition, also non-food allergic consumers should accept novel foods to be available for consumption.

## 6.1 Summary and conclusions

In chapter 2 of this thesis, the issues around novel foods and food allergies at the start of this research were reviewed. The first issue emerging from the literature review concerns the prevalence of food allergy. Although an increasing food allergy prevalence is frequently mentioned in food allergy literature, there is no agreement regarding the prevalence. This lack of agreement may be due to the difficulty in diagnosing food allergy, or to the varying definitions of food allergy that are used. One distinction in food allergy that can be made is that between 'true' food allergy and perceived food allergy. 'True' food allergy refers to a formal diagnosis of food allergy, whereas 'perceived' food allergy refers to the people's belief that they personally exhibit the symptoms of a food

allergy, independent of whether a health professional would diagnose them as food allergic. There is general agreement that food allergy prevalence is higher in children than in adults because of an increased predisposition if children to develop food allergy and by the tendency of children to develop immunologic tolerance as they get older (Sampson, 1999b).

Food allergies can have a significant impact on the quality of life and economic functioning of people who suffer from them, as well as wider implications for society more generally. Direct costs of food allergy include medical costs, whereas indirect costs are linked to factors such as work and productivity (Gergen, 2001). The latter have a much greater effect on individuals and families because these costs reflect the functioning and quality of life of the individual and his family. It is important to realise that the impact of food allergy on daily lives of food allergic consumers is not only a direct result from the disease and its symptoms, but also from the treatment: avoidance of the problematic foods. Restriction or complete elimination diets and emergency management of allergic reactions are at the time of writing the only reliable therapy to treat food allergy. This has a negative impact on quality of life.

Another important issue relates to both the risks and the benefits associated with the introduction of novel foods. One potential benefit of novel foods is that of hypoallergenicity, although there is the potential risk that new proteins are introduced into the human food chain together with the novel foods. Consumer acceptance of novel foods is contingent on technical risk estimates, and consumer perceptions of risks and benefits. An important finding from literature was the concept of risk conflict, which refers to the differences between the way that experts and non-experts evaluate risks (Slovic, 1999). Technical risk assessments are often used by experts and regulators to determine acceptable safety levels (Taylor and Hefle, 2001), although consumer decision-making is, in part, based on broader, societally relevant factors of concern (Frewer et al., 2004). People may tolerate some level of risk if they also perceive direct benefit (Frewer et al., 2003b). Novel foods with reduced or absent allergenicity may be perceived as beneficial by food allergic consumers and therefore acceptable. For non-food allergic consumers, the perceived risks may outweigh the benefits. Chapter 2 concludes that hypoallergenic novel foods, despite some uncertainty regarding the (hypo)allergenic potential, may contribute to food allergy management, by aiding food allergen avoidance.

Because of the different perceptions concerning risks among experts and consumers, chapter 3 looks at whether novel foods can be used as allergy management strategy from both a stakeholder and food allergic consumer perspective. Stakeholder opinions (collected using semi-structured interviews) regarding the acceptability of

hypoallergenic novel foods were assessed. The opinions of food allergic consumers were collected during three focus group discussions (one comprising of anaphylactic food allergic consumers, and two comprising of consumers with less severe food allergies). Optimising a food allergy management strategy that involves the application of (hypoallergenic) novel foods is contingent on both stakeholder and consumer acceptance of novel foods and associated production processes where relevant.

Most stakeholders believed that novel foods can, in theory, contribute to a solution for the food allergy problems they described because the novel foods can be hypoallergenic, and therefore they may represent a safe alternative for food allergic consumers. Natural novel foods are only a good alternative when the products are proven safe, but initially stakeholders considered them more as a cause of consumer's food allergy problems. The stakeholders also mentioned some potential problems when novel foods are introduced, such as consumers who develop allergies to the novel proteins in novel foods. They also stressed that novel foods can only be effective as food allergy management strategy if consumers are willing to buy them. Food allergic consumers would be in favour of hypoallergenic novel foods being developed and commercialised. However, they did express doubts regarding the reduced allergenicity of such novel foods. Consumers perceived that novel foods could only be used as allergy management strategy when all allergenic food ingredients are replaced across all food chains completely. An advantage of hypoallergenic novel foods according to the food allergic consumers is that these novel foods could prevent or delay the development of new allergies because they are exposed to reduced levels of allergens. Both stakeholders and food allergic consumers expressed some enthusiasm for the introduction of truly hypoallergenic novel foods. Whilst the results suggest that hypoallergenic novel foods may be acceptable to food allergic consumers, consumers expressed the view that a 'cure' for food allergy is preferred over substituting existing foods with hypoallergenic alternatives.

Chapter 4 identifies consumer attitudes towards novel foods and assesses the impact of information about food allergy and novel foods on non-food allergic consumer acceptance, and thus if food developers and policy makers should be encouraged to invest in low allergen novel foods. The results show that hypoallergenic novel food acceptance as allergy management is more acceptable to consumers who perceive high benefits and low or medium risks. Many food allergic consumers did not perceive the benefits of hypoallergenic novel foods to be high and were less accepting of hypoallergenic novel foods as allergy management strategy. Both food allergic consumers and non-food allergic consumer acceptance of novel foods was higher for natural novel foods compared to genetically modified novel foods. It is concluded that the

application of novel foods as an allergy management strategy is complicated by the fact that many of the consumers who are supposed to experience the benefits of these novel foods are less likely to accept the novel foods.

Chapter 5 reviews the existing legislation associated with the introduction of novel foods and assesses the efficacy of such legislation with respect to allergy risks and benefits. Various regulations are in place to protect consumer health. These regulations require novel food safety to be assessed before they can enter the market. However, the current regulatory frameworks do not specify how these assessments should be performed. The EU recommends which information is needed for a novel food application, but besides from mentioning that allergenicity information is required, it is not specified how this allergenicity assessment should be performed. This may relate to the fact that the safety assessment methods available and best suited depend on the type of novel food under assessment. None of the safety assessments include benefits assessment. However, when a hypoallergenic novel food with benefits for food allergic consumers is being evaluated, it can be argued that information about the potential benefits should be formally included in management decisions and therefore the assessment of benefits would be helpful. It is concluded that including a benefit assessment in the novel food legislation, may increase acceptability.

### 6.2 Novel foods as allergy management strategy

Food allergy is an important health issue. The results from both the consumer focus group discussions and the literature review make this clear. In particular the impact on quality of life of food allergic consumers is significant due to the consequences for their daily lives, such as affects meal preparation activities in the home, reduced social activities (for both parents and children), and anxiety and stress. The time and effort that it takes to provide a safe environment for food allergic children has potential to cause a significant impact on daily life. This calls for a food allergy management strategy that eases the burden on food allergic consumers. The research presented in this thesis focussed on the contribution that novel foods may make to such a food allergy management strategy. Figure 6.1 presents an overview of the main concepts in this thesis and how they relate to food allergy management. The following sections discuss how these concepts relate to food allergy management.

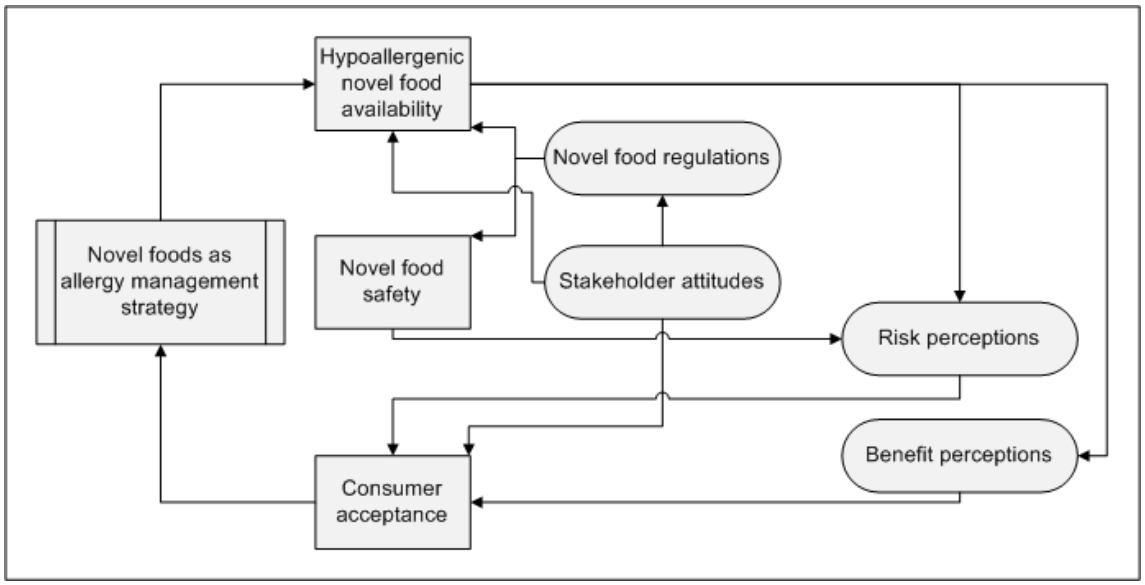


Figure 6.1 Important concepts of novel foods as part of a food allergy management strategy.

Food allergy management

Food allergy management consists of two strategies, which are related to the two phases of the development of food allergy. This first strategy aims at preventing the development of a food allergy, and desensitising food allergic consumers, once they have been sensitised. The second strategy aims at preventing the occurrence of food allergy symptoms. This can be achieved by allergen avoidance. Hypoallergenic novel foods may play a role in both food allergy management strategies.

Some indications exist that treatment with a hypoallergenic fragment of cow's milk may prevent the onset of sensitisation to cow milk (Herz, 2008). This implies that some hypoallergenic novel foods could contribute to inducing immunological tolerance. However, whether early introduction of potential allergens, in forms with reduced allergenic potential, such as hypoallergenic novel foods, is helpful remains to be proven (Skripak and Sampson, 2008). The application of novel foods as desensitisation therapy was not recognised by the stakeholders nor by the food allergic consumers in this research. They did recognise the (theoretical) possibility of hypoallergenic novel foods to facilitate allergen avoidance, although this possibility may be limited in practice. Obviously hypoallergenic novel foods need to be available to consumers to be able to have such effects. This is indicated by the arrow from 'novel foods as allergy management strategy' to 'hypoallergenic novel foods availability'.

During the research presented in this thesis, no hypoallergenic novel foods could be identified and therefore, strictly speaking, novel foods are not likely to be beneficial for food allergic consumers. This does not mean that no further efforts should be made to

develop novel foods since other (consumer) benefits could be present. Further, some hypoallergenic new foods may exist that fall outside the definition of novel foods as stated in EU legislation. An example of such a food is the Santana apple (Kootstra et al., 2007), which is new food and marketed as hypoallergenic. It is difficult to systematically identify these new foods. Other examples of hypoallergenic foods are the “delicious soybean” and “TUSC-1 wheat”, which are approved in Canada under Canadian novel food legislation. The modifications of these foods aimed to improve organoleptic or technical properties, but these also resulted in reduced levels of major allergenic proteins. This indicates that there may be hypoallergenic new foods available that can be used as part of allergy management strategies, although these food may not be marketed as hypoallergenic. This shows that hypoallergenic novel food availability is also influenced by stakeholder attitudes, such as the food industry who may decide to market a product as hypoallergenic.

Besides the introduction of hypoallergenic novel foods to facilitate allergen avoidance, other measures can be identified to be applicable in allergy management strategies, such as improved information provision to a food allergic individual about the specific food allergy and its management, better diagnostic techniques that provide food allergic individuals with information about which allergens to avoid, and improved allergen traceability and allergen labelling which allows food allergic consumers to effectively avoid allergens (Mills, 2007).

Novel food safety and uncertainty

(Hypoallergenic) novel foods have to be safe. Not only for consumers in general, but also for food allergic consumers. The safety is novel foods is addressed in novel food legislation. (In figure 6.1 this is indicated by the arrow from novel food regulations to novel food safety.) Novel food legislation requires novel food safety to be assessed before novel foods are allowed onto the market. Although novel food legislation recognises other types of novel foods besides genetically modified novel foods, it does not state how the safety of these novel foods should be assessed. The currently available assessment procedures are best suited to assess the safety of novel proteins. This means that the safety of genetically modified novel foods and novel proteins can be adequately assessed. It should be noted that the result of an allergenic safety assessment procedure is a conclusion as to the likelihood of a food being allergenic. This means that some uncertainty remains regarding the allergenic safety of the novel food.

Novel food regulations also affect the availability of hypoallergenic novel foods. This is indicated in figure 6.1 by the arrow from ´novel food regulations´ to

´hypoallergenic novel food availability´. It is important to realise that any available hypoallergenic novel food can be considered as safe, (otherwise regulations would prevent the novel food from being allowed onto the market) but not every safe novel food is hypoallergenic. Hypoallergenicity refers to the elimination, or removal of the biological activity of allergens (Herz, 2008). This means that hypoallergenic novel foods contain less allergen, quantitatively or qualitatively, than non-hypoallergenic novel foods. The benefit of novel hypoallergenic foods is that they can be safer than conventional products. A product that is only reasonably safe is less likely to have such benefits. Dearman & Kimber (2009) report that the outcome of the risk assessment procedure will be a decision as to whether accept, reject, or label the particular novel food (Dearman and Kimber, 2009). In the case when hypoallergenic novel foods are to be applied as allergy management strategy, (precautionary) labelling of potentially allergenic products is not acceptable. For hypoallergenic novel foods as allergy management strategy to be acceptable to food allergic consumers it is necessary that food allergic consumers get as much certainty as possible about the remaining allergenicity of the novel food product. Considering that absolute certainty about hypoallergenicity is not possible this (un)certainty regarding the hypoallergenicity of novel foods needs to receive special attention in case novel foods are applied as part of allergy management. The relation between hypoallergenic novel food availability and consumer acceptance is presented in figure 6.1 by arrows through risk and benefit perceptions. These perceptions are also influence by the uncertainty about the (hypo)allergenicity of novel foods.

Further, it is interesting to note that rational decision making may increase awareness of uncertainty by drawing attention to the lack of better data (Hu et al., 2005). When there is heightened sensitivity to risk as in the case of food allergic consumers, certain recommendations regarding novel food use as part of an allergy management strategy may thus increase the experience of uncertainty. This should be taken into account when communicating the potential benefits of novel foods to food allergic consumers and requires more research to determine the best communication strategy.

Consumer concerns regarding allergenicity of novel foods focus on hidden allergens and less on cross-reactivity and de-novo sensitisation. It is the avoidance of allergens that concerns them. That is why the potential allergen content of novel foods is of particular importance to them. It is technically possible to test the newly introduced allergen content of all novel foods, although in the case of natural novel foods, for which not all proteins have been identified, this may be expensive. If most cross-reacting allergens have been identified, then the uncertainty regarding the presence of cross-reacting allergens in novel foods becomes relatively small. Considering that cross-reactivity is not a major concern to food allergic consumers, this means that novel foods

for which cross-reaction safety cannot be guaranteed could still be acceptable to food allergic consumers.

Food allergic consumers

The successful application of hypoallergenic novel foods depends on consumer acceptance of these novel foods (indicated with the arrow from ´consumer acceptance´ to ´novel foods as allergy management strategy´ in figure 6.1). Most food allergic consumers expressed some enthusiasm during the focus group discussions about the application of novel foods as allergy mitigation strategy. These results were not confirmed during the consumer acceptance study, presented in chapter 4, which showed low acceptance of hypoallergenic novel foods among food allergic consumers. A first reason for this lack of confirmation could be that the problems associated with food allergy, include more than those that can be influenced by hypoallergenic novel foods. For example, the most problematic aspect of food allergy is avoiding foods that may contain allergens. It is important to note that introducing hypoallergenic novel foods does not change the number of food products that need to be avoided, unless the allergenic foods and ingredients are completely replaced with hypoallergenic alternatives, which is not a likely solution. Therefore, hypoallergenic novel foods may be more effective as allergy management strategy when they serve as replacement for allergenic foods that are easy to recognise and to avoid. It can be reasoned that because of this, the stress and anxiety related to the difficulties associated with allergen avoidance of widely used allergens is not reduced. Food allergic consumers are more positive about novel food innovations than food allergic consumers. This is the opposite of what had been expected at the start of the research. Food allergic consumer attitudes towards hypoallergenic novel foods were expected to be more positive than those of non-food allergic consumers because the former might experience benefits from hypoallergenic novel foods. A second reason for the lower consumer acceptance of novel foods may be that food allergic consumers have their daily lives and food allergy under control, which took them a lot of effort. When hypoallergenic novel foods are introduced, their situation changes and they need to adjust to those changes. This may make them more sceptical to any suggested food allergy management strategy that is not a cure. A third reason could be that the food allergic consumers are more cautious regarding the consumption of new foods, adopting a risk avoidance strategy, even if these risks are not perceived to be high. Hypoallergenic novel foods could offer food allergic consumers a wider food choice. This also becomes clear when looking at a food allergy quality of life questionnaire, which includes many aspects of quality of life that can be affected by food allergy (Flokstra-De Blok et al., in press). Theoretically, novel foods can only influence a

limited number of these items of quality of life. Therefore, the theoretical contribution of novel foods in improving quality of life is also limited. Quality of life of food allergic consumers is affected by many other factors than the foods they need to avoid and the foods that are available to them, such as their social environment. Novel foods are not likely to influence these social problems. This limitation may influence benefit perceptions of hypoallergenic novel foods, which may explain the low consumer acceptance of novel foods. Previous research shows that benefit perceptions are an important determinant of consumer acceptance. The willingness to purchase GM food is higher for low-allergen foods than for novel foods with no specified consumer benefit (Miles et al., 2006a). Health benefits are important, but they need to be specified to improve consumer acceptance. Apparently, some food allergic consumers perceive that the benefits from hypoallergenic novel foods outweigh the perceived risk and therefore are reluctant to accept novel foods.

Some food allergic consumers may benefit more from the introduction of hypoallergenic novel foods as allergy management strategy than other food allergic consumers. It is not likely that all allergenic foods and ingredients in the food chain will be replaced with hypoallergenic counterparts. Therefore, consumers with an allergy to, for example, apple can now buy the non-allergenic apple Santana. The Santana apple (although strictly speaking not a novel food) does have benefits for consumers with an apple allergy. Some of these consumers can eat an apple again and these people are enthusiastic about this apple. This indicates that some hypoallergenic foods can have benefits for food allergic consumers. For food allergic consumers for whom food allergen avoidance is particularly difficult because they are allergic to an allergen that is used in many food products, like milk or wheat, replacement of this ingredient by a hypoallergenic counterpart is not a likely option. The relative contribution of hypoallergenic novel foods to a food allergy management strategy is therefore larger for consumers with an allergy to products that are easy avoidable. The relative contribution of novel foods to improving quality of life is therefore limited, but a positive effect can be expected, nevertheless.

Another issue relating to the introduction of hypoallergenic novel foods into the food chain is acceptance by non-food allergic consumers. They do accept novel foods with specific benefits for food allergic consumers.

When discussing the possibilities of applying hypoallergenic novel foods as allergy management strategy, it is important to realise that food allergic consumers prefer the development of a cure for food allergy over the development of hypoallergenic novel foods. This finding is in line with existing literature that states that prevention of disease should always be the first and foremost objective (Skripak and Sampson, 2008). When

making decisions about the allocation of future research funds, this should be taken into account. However, since at the time of writing the treatment options are limited to avoidance of the problematic foods and therefore facilitating food allergen avoidance through the introduction of hypoallergenic novel foods may be effective as part of an allergy management strategy.

### 6.3 Practical implications

The results presented in this thesis provide food allergic consumers with information regarding the introduction of hypoallergenic novel foods as part of food allergy management. The benefits associated with such a management strategy are expected to differ between food allergic consumers. Consumers who are allergic to allergens that are not present in many different products in the food chain are expected to benefit more from the introduction of hypoallergenic novel foods than consumers who are allergic to food ingredients that are used in many different products. In addition, it is important to realise that food allergies affect many aspects of food allergic consumers´ daily lives, such as the disbelief of the social environment and that hypoallergenic novel foods cannot improve all those. However, for some food allergic consumers hypoallergenic novel foods may become a valuable part of their food allergy management.

The results also show that although the novel foods that are developed were not intended to be used as part of an allergy management strategy, there were some examples that appeared to be hypoallergenic. This implies that the food industry could benefit additionally from the development of novel foods, if those are evaluated for potential hypoallergenicity as well.

The implications of this research for regulators are related to the potential benefits of hypoallergenic novel foods. Current novel food regulations are limited to the assessment of the safety of the novel foods. However, including the assessment of hypoallergenicity as benefit to the safety evaluation of novel foods would provide more certainty about the hypoallergenicity of novel foods to food allergic consumers, especially when the scientific community develops reliable (hypo)allergenicity assessment methods.

Since at the time of writing no hypoallergenic novel foods are available and their potential contribution to food allergy management is expected to be limited, it is not likely that health professionals can recommend food allergic consumers to include hypoallergenic novel foods in their diet.

### 6.4 Research limitations and future research

This research focussed on the application of novel foods as allergy management strategy. Since no hypoallergenic novel foods were available at the time this research was conducted, therefore it was not possible to perform an experiment in which food allergic consumers use hypoallergenic novel foods for a longer period of time, and quality of life is measured before and after this period of hypoallergenic novel food use. This means that the current research remains hypothetical. When in the future, hypoallergenic novel foods are available, it is recommended that an experiment is performed to test the hypothesis that hypoallergenic foods can influence quality of life. Further, including hypoallergenic foods that do not fall under the novel food regulation may provide useful insights into the possibilities of applying hypoallergenic foods as allergy management strategy.

This thesis focussed on novel foods as part of a daily diet. Current research also focuses on the application of novel food proteins to allergen immunotherapy (Burks et al., 2008; Patriarca et al., 2009). It can be argued that when trying to achieve immunological tolerance to allergens the hypoallergenic novel foods have a more therapeutic function. While consumers do not perceive many benefits of hypoallergenic novel foods and their use in daily life, they may be more positive for these novel foods to be used therapeutically. Before hypoallergenic novel foods can be used as a therapeutic methods, it is advised that future research addresses consumer acceptance of novel foods as therapeutic method. Consumer acceptance of novel foods as therapy may be complicated by the fact that consumers will be exposed to doses of allergen, which may cause allergic reactions. However, it can be expected that consumer acceptance of novel foods is higher when they are applied as a therapy, since consumers expressed a preference for a cure for food allergy.

Although some food allergic consumers indicate that the price of hypoallergenic novel foods should be comparable to traditional foods, others indicate that they are willing to pay an increased price for these hypoallergenic novel foods (Cornelisse-Vermaat et al., 2008a). The extend to which food allergic consumers are willing to pay more for hypoallergenic foods with benefits to them could be subject of future research, once hypoallergenic foods with benefits for food allergic consumers have been identified.

Novel foods may have more benefits for people who have recently been diagnosed and who need to learn how to deal with their food allergy, compared to food allergic consumers who have adjusted to living with a food allergy. Recently diagnosed food allergic consumers may benefit from a wider product choice when hypoallergenic

foods are available. Future research could focus on this aspect of hypoallergenic novel foods as allergy management strategy.

### 6.5 Final conclusion

This thesis has provided insight into the possibilities and limitations of applying novel foods as part of an allergy management strategy. This research contributes to a better understanding of the impact of food allergy on daily life of food allergic consumers and shows that hypoallergenic novel foods may improve food allergen avoidance because food allergic consumers will have more foods to choose from. In addition, non-food allergic consumers appear to be willing to accept novel foods in case those have benefits for food allergic consumers.

The results of this thesis provide the food industry and regulators with important insights into the application of novel foods as allergy management strategy, enabling them to better respond to food allergic consumer needs regarding dealing with their food allergy. The food industry should pay attention to potential hypoallergenicity of newly developed foods, since the results in this thesis showed some examples of hypoallergenic foods that were not marketed as such. Regulators should include potential hypoallargenicity as part of a benefit assessment to the safety assessment of novel foods, to provide consumers and other stakeholders with as much certainty regarding remaining allergenicity as possible.

This thesis has extended existing research about novel foods and food allergy, and focussed on the introduction of hypoallergenic novel foods as part of an allergy management strategy. The results show that although hypoallergenic novel foods can facilitate allergen avoidance, their influence remains limited because many other factors, such as the recognition of their allergy by their social environment cause the food allergy problems. Nevertheless, considering that the food allergy management options are limited, the contribution that hypoallergenic novel foods, which can be replacement for allergenic foods may be valuable for consumers who are allergic to foods that are easy to recognise and avoid.

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# Summary

Food allergy is an important health issue. It is defined as an inappropriate immunological reaction to normally harmless food components and affects 5-8% of children and 1-2% of adults. At the time of writing, the only reliable treatment of food allergy is strict avoidance of the problematic foods. Food allergy can have a profound impact on quality of life and economic functioning of food allergic consumers and their families, not only because of the immediate clinical effects related to an individual's allergic condition, but also because of the alterations in daily life that have to be made to prevent the occurrence of symptoms.

The introduction of novel foods is of interest to the management of food allergy for two reasons. On the one hand, the development and introduction of novel hypoallergenic foods represents a potential approach to reducing the negative health impacts of food allergy. On the other hand, the introduction of novel proteins into the food chain and the human diet may result in new cases of food allergy. *Novel foods* are defined as foods or food ingredients that have no history of safe use in the European Union (EU). The absence of a history of safe use can be the result of: (1) genetic modification of the food or production of the food using genetically modified organisms, (2) novel processing techniques, or (3) the food being new to the European Union.

The research presented in this thesis explores whether novel foods can be used as part of an allergy management strategy. For novel foods to be used in food allergy management various factors must be considered. These include (1) the actual hypoallergenicity of novel foods, (2) consumer acceptance of novel foods in general and by food allergic consumers in particular, and (3) the potential impact of novel foods on the quality of life of food allergic consumers.

In chapter 2 literature is reviewed to identify the issues associated with novel foods and food allergy. Food allergies can have a significant impact on the quality of life and economic functioning of people who suffer from them, as well as wider implications for society more generally. Direct costs of food allergy include medical costs, whereas indirect costs are linked to factors such as work and productivity. The latter have a much greater effect on individuals and families because these costs reflect the functioning and quality of life of the individual and his family. It is important to realise that the impact of food allergy on daily lives of food allergic consumers is not only a direct result from the disease and its symptoms, but also from the treatment: avoidance of the problematic foods. Restriction or complete elimination diets and emergency management of allergic reactions are at the time of writing the only reliable therapy to treat food allergy.

Another important issue is that there are both risks and benefits associated with the introduction of novel foods. Consumer acceptance of novel foods is contingent on technical risk estimates, and consumer perceptions of risks and benefits. An important finding from literature was the concept of risk conflict, which refers to the differences between the way that experts and non-experts evaluate risks. Technical risk assessments are often used by experts and regulators to determine acceptable safety levels, although consumer decision-making is, in part, based on broader, societally relevant factors of concern. People may tolerate some level of risk if they also perceive direct benefit. Novel foods with reduced of absent allergenicity may be perceived as beneficial by food allergic consumers and therefore acceptable. For non-food allergic consumers, the perceived risks may outweigh the benefits. Chapter 2 concludes that hypoallergenic novel foods, despite some uncertainty, have the potential to contribute to food allergy management, by aiding food allergen avoidance. However, it remained unclear what the allergy risks of novel foods are.

Because of the different perceptions concerning risks among experts and consumers, chapter 3 looked at whether novel foods can be used as allergy management strategy from both a stakeholder and food allergic consumer perspective. Most stakeholders believed that novel foods can, in theory, contribute to a solution for the food allergy problems they described because the novel foods can be hypoallergenic, and therefore they may represent a safe alternative for food allergic consumers. The stakeholders also mentioned some potential problems when novel foods are introduced, such as consumers who develop allergies to the novel proteins in novel foods. They also stressed that novel foods can only be effective as food allergy management strategy if consumers are willing to buy them. Food allergic consumers would be in favour of hypoallergenic novel foods being developed and commercialised. However, they did express doubts regarding the reduced allergenicity of such novel foods. Consumers perceived that novel foods could only be used as allergy management strategy when all allergenic food ingredients are replaced across all food chains completely. Both stakeholders and food allergic consumers expressed some enthusiasm for the introduction of truly hypoallergenic novel foods. Whilst the results suggest that hypoallergenic novel foods may be acceptable to food allergic consumers, consumers expressed the view that a ‘cure’ for food allergy is preferred over substituting existing foods with hypoallergenic alternatives.

In chapter 4 consumer attitudes towards novel foods are identified and the impact of information about food allergy and novel foods on non-food allergic consumer acceptance is assessed. The results show that hypoallergenic novel food acceptance as allergy management is more acceptable to consumers who perceive high benefits and

low or medium risks. Many food allergic consumers did not perceive the benefits of hypoallergenic novel foods to be high and were less accepting of hypoallergenic novel foods as allergy management strategy. Both food allergic consumer and non-food allergic consumer acceptance of novel foods was higher for natural novel foods compared to genetically modified novel foods. It is concluded that the application of novel foods as an allergy management strategy is complicated because many of the consumers who are supposed to experience the benefits of these novel foods are less likely to use these novel foods.

Chapter 5 reviews the existing legislation associated with the introduction of novel foods and assesses the efficacy of such legislation with respect to allergy risks and benefits. Various regulations are in place to protect consumer health. These regulations require novel food safety to be assessed before they can enter the market. However, the current regulatory frameworks do not specify how these assessments should be performed. This may relate to the fact that the safety assessment methods available and best suited depend on the type of novel food under assessment. None of the safety assessment include benefits assessment. However, when a hypoallergenic novel food with benefits for food allergic consumers is being evaluated, it can be argued that information about the potential benefits should be formally included in management decisions and therefore the assessment of benefits would be helpful.

Overall, the results in this thesis suggest that the potential contribution of novel foods as part of an allergy management strategy is limited. The first reason for this conclusion is that no hypoallergenic novel foods could be identified. However, it is possible that some hypoallergenic new foods exist that fall outside the definition of novel foods as used in this thesis. The second reason concerns the limited influence that can be expected of novel foods. The most important factor affecting quality of life of food allergic consumers is the avoidance of food allergens. Application of hypoallergenic foods through the food chain is necessary to reduce the number of food products that food allergic consumers need to avoid. However, replacement of all allergenic foods and ingredients through the food chain is not likely. This implies that only novel foods that are not used as ingredient in many other foods can be used to replace allergenic foods. In general, the foods that are not used as an ingredient in many other products are easier to avoid. A third reason for the limited potential of hypoallergenic novel foods to be used as allergy management strategy concerns the uncertainty regarding the results of the allergenicity assessment, which always are a conclusion as to the likelihood of a food being an allergen. For a food to be applied as part of an allergy management strategy as much certainty as possible is required, especially for food allergic consumers who will experience severe life threatening symptoms when exposed to food allergens. However,

considering the limited number of allergy management strategies, it can be argued that any contribution, including hypoallergenic novel foods, to food allergy management would be welcomed.

Overall, this research contributes to a better understanding of the impact of food allergy on daily lives of food allergic consumers and shows that hypoallergenic novel foods may improve certain aspects of daily lives of some food allergic consumers, through improved allergen avoidance. The results of this thesis provide the food industry and regulators with important insights into the application of novel foods as allergy management strategy, enabling them to better respond to food allergic consumer needs regarding dealing with their food allergy.

# Samenvatting (Dutch summary)

Voedselallergie is een belangrijk gezondheidsprobleem. Voedselallergie is gedefinieerd als een misplaatste immunologische reactie op voedsel dat bij niet allergische consumenten geen schadelijke reactie veroorzaakt. Ongeveer vijf tot acht procent van de kinderen en een tot twee procent van de volwassenen hebben last van een voedselallergie. Op het moment van dit schrijven is de enige behandelmogelijkheid voor mensen met een voedselallergie het strikt vermijden van de problematische voedingsmiddelen. Voedselallergie kan een grote invloed hebben op de kwaliteit van leven van consumenten met een voedselallergie en hun gezin. Daarnaast heeft een voedselallergie vaak ook financiële gevolgen. Niet alleen vanwege de directe klinische gevolgen van de allergische aandoening, maar ook door de aanpassingen die in het dagelijkse leven gedaan moeten worden om allergische symptomen te voorkomen.

De introductie van 'novel foods' is interessant wat betreft het beheersen van voedselallergieën om twee redenen. Enerzijds biedt de ontwikkeling en introductie van hypoallergene 'novel foods' een potentiële benadering om de negatieve gevolgen van voedselallergie te beperken. Anderzijds kan de introductie van nieuwe eiwitten in de voedselketen en het dieet van mensen resulteren in nieuwe voedselallergieën. 'Novel foods' worden gedefinieerd als voedingsmiddelen, of voedingsingrediënten die geen verleden hebben van veilig gebruik in de Europese Unie (EU). The ontbreken van dat verleden kan het gevolg zijn van: (1) genetische modificatie van het voedsel, of een productiewijze waarbij genetisch gemodificeerde organismen worden gebruikt, (2) toepassing van nieuwe bewerkingsmethoden, of (3) het voedsel is nieuw in de EU.

Het onderzoek dat in dit proefschrift wordt gepresenteerd verkent of 'novel foods' gebruikt kunnen worden als onderdeel van een allergiemanagementstrategie. Voordat 'novel foods' gebruikt kunnen worden als voedselallergie management moet rekening gehouden worden met een aantal factoren, zoals (1) de hypoallergeniciteit van de 'novel foods', (2) consumenten acceptatie van 'novel foods' in het algemeen en door consumenten met een voedselallergie in het bijzonder en (3) de potentiële invloed van 'novel foods' op de kwaliteit van leven van voedselallergische consumenten.

In hoofdstuk 2 is literatuur bestudeerd om de kwesties gerelateerd aan 'novel foods' en voedselallergie te identificeren. Voedselallergieën kunnen een aanzienlijke invloed hebben op de kwaliteit van leven en de financiële situatie van mensen met een voedselallergie. Daarnaast kunnen ze ook gevolgen hebben voor de hele samenleving. Directe kosten van voedselallergie zijn medische kosten. De indirecte kosten zijn gerelateerd aan werk en productiviteit. Indirecte kosten hebben een groter effect op

individuele consumenten en de mensen in hun omgeving. Het is belangrijk te beseffen dat de invloed van voedselallergie op het dagelijkse leven van consumenten met een voedselallergie geen direct gevolg is van de ziekte en de symptomen, maar vooral een gevolg is van de behandelwijze: het vermijden van problematische voedingsmiddelen. Het beperken of compleet elimineren van de inname van specifieke voedingsmiddelen en het behandelen van allergische reacties in noodgevallen zijn op het moment van dit schrijven de enige betrouwbare behandelmethode voor voedselallergie. Een belangrijke kwestie omtrent de introductie van 'novel foods' is dat er zowel risico's als voordelen aan verbonden zijn. Consumentenacceptatie van 'novel foods' is afhankelijk van technische risicoschattingen en het beeld dat consumenten hebben van de risico's en voordelen. Een belangrijke resultaat van de literatuurstudie is het concept van 'risk conflict' dat refereert aan de verschillende manieren waarop experts en leken risico's beoordelen. Technische risicobeoordelingen worden vaak gebruikt door experts en wetgevers om acceptabele veiligheidsniveaus te bepalen, terwijl consumentenbeslissingen deels gebaseerd zijn op bredere sociale factoren. Mensen accepteren wellicht een bepaald risico indien zij ook direct voordeel hebben. Voedselallergische consumenten kunnen het beeld hebben dat 'novel foods' met verminderde of geen allergeniciteit voordelen hebben voor hen en daardoor deze voedingsmiddelen accepteren. Voor consumenten zonder voedselallergie kan het beeld van de risico's van deze voedingsmiddelen zwaarder wegen dan hun beeld van de voordelen. Hoofdstuk 2 concludeert dat hypoallergene voedingsmiddelen mogelijk een bijdrage kunnen leveren aan voedselallergie management, ondanks enige onzekerheid, doordat het vermijden van allergenen vergemakkelijkt wordt. Het blijft onduidelijk wat de risico's van 'novel foods' zijn.

Vanwege de verschillende beeldvormingen van de risico's van 'novel foods' bij experts en consumenten bekeek hoofdstuk 3 of 'novel foods' gebruikt kunnen worden om voedselallergieën te beheersen vanuit het standpunt van experts en voedselallergische consumenten. De meeste experts geloofden dat 'novel foods' in theorie een bijdrage kunnen leveren aan een oplossing voor de voedselallergieproblematiek zoals zij die beschreven, doordat 'novel foods' mogelijk hypoallergeen zijn en daardoor een veilig alternatief kunnen bieden aan consumenten met een voedselallergie. De experts beschreven ook een aantal mogelijke problemen die kunnen ontstaan bij de introductie van 'novel foods' zoals het ontwikkelen van een allergie voor eiwitten in deze 'novel foods'. Ze benadrukten ook dat 'novel foods' alleen effectief kunnen zijn als voedselallergiemanagement indien consumenten bereid zijn de 'novel foods' te kopen. Voedselallergische consumenten waren voorstander van de ontwikkeling en verkoop van hypoallergene voedingsmiddelen. Zij twijfelden wel of 'novel foods' daadwerkelijk hypoallergeen zouden kunnen zijn. Ze gaven aan dat 'novel foods'

alleen gebruikt kunnen worden als allergiemanagement als alle allergene varianten van dat product vervangen zouden worden in de gehele voedselketen. Zowel de experts als de consumenten waren in enige mate enthousiast over de introductie van hypoallergene voedingsmiddelen. Hoewel de resultaten laten zien dat hypoallergene 'novel foods' geaccepteerd zouden worden door voedselallergische consumenten geven deze consumenten de voorkeur aan het genezen van hun voedselallergie.

In hoofdstuk 4 werden consumentenattitudes ten aanzien van 'novel foods' geïdentificeerd. Daarnaast werd de invloed van informatie over het hebben van een voedselallergie en 'novel foods' op acceptatie door consumenten zonder voedselallergie bekeken. De resultaten laten zien dat acceptatie van hypoallergene 'novel foods' groter is bij consumenten die veel voordelen zien en weinig of gemiddelde risico's. Veel voedselallergische consumenten zagen geen of weinig voordelen van 'novel foods' en hun acceptatie van hypoallergene 'novel foods' was lager. Zowel consumenten met een voedselallergie als ook consumenten zonder voedselallergie vonden natuurlijke 'novel foods' meer acceptabel dan genetisch gemodificeerde 'novel foods'. De conclusie is dat de toepassing van 'novel foods' als allergiemanagement strategie gecompliceerd is vanwege het feit dat juist die consumenten die verwacht werden voordelen te ervaren van 'novel foods', het minst geneigd zijn de producten te gebruiken.

Hoofdstuk 5 bekeek de huidige 'novel food' regelgeving en beoordeelt de doeltreffendheid van die regelgeving met betrekking tot allergierisico's en -voordelen. Verscheidene wet- en regelgeving bestaat met als doel de gezondheid van consumenten te beschermen. Deze stellen dat de veiligheid van 'novel foods' beoordeeld moet worden voordat ze op markt toegelaten kunnen worden. De huidige wet- en regelgeving stelt niet hoe die veiligheid bepaald moet worden. Dit kan te maken hebben met het feit dat de beschikbare en meest geschikte methodes om de veiligheid te beoordelen afhankelijk zijn van het type 'novel food' dat beoordeeld moet worden. Geen van de veiligheidsbeoordelingen omvatten ook een beoordeling van de mogelijke voordelen. Indien een hypoallergeen 'novel food' met voordelen voor consumenten met een voedselallergie beoordeeld wordt, is het niet ondenkbaar dat informatie over de potentiële voordelen meegenomen moet worden in management besluiten. Hierbij zou een formele beoordeling van de voordelen behulpzaam zijn.

De resultaten in dit proefschrift suggereren dat de potentiële bijdrage van 'novel foods' aan voedselallergiemanagement beperkt is. De eerste reden voor deze conclusie is dat geen hypoallergene 'novel foods' lijken te bestaan. Desalniettemin is het mogelijk dat hypoallergene nieuwe voedingsmiddelen bestaan die niet onder de definitie van 'novel foods' vallen, zoals die in dit proefschrift gehanteerd is. De tweede reden betreft de beperkte invloed van 'novel foods' op de voedselallergieproblematiek. Kwaliteit van

leven wordt het meest beïnvloed door de hoeveelheid voedingsmiddelen die vermeden dient te worden. Het introduceren van hypoallergene voedingsmiddelen in de voedselketen, waarbij de allergene producten vervangen worden is noodzakelijk om het aantal voedingsmiddelen dat voedselallergische consumenten dienen te vermijden te verminderen. Het is echter niet waarschijnlijk dat alle allergene producten in de voedselketen vervangen kunnen worden door hypoallergene varianten. Dit betekent dat slechts 'novel foods' die niet als ingrediënt in veel andere producten gebruikt worden gebruikt kunnen worden als vervanging. Een derde reden voor de beperkte mogelijkheden hypoallergene 'novel foods' als allergiemanagement strategie te gebruiken betreft de onzekerheid over de resultaten van de allergeniciteitsbeoordeling. Deze geven slechts een indicatie van de waarschijnlijkheid dat een eiwit een allergeen is. Voordat een voedingsmiddel gebruikt kan worden als onderdeel van een voedselallergiemanagementstrategie moet zoveel mogelijk zekerheid bestaat over de resterende allergeniciteit. Dit geldt in het bijzonder voor voedselallergische consumenten die levensbedreigende symptomen krijgen als zij blootgesteld worden aan allergenen. In aanmerking genomen dat er slechts weinig voedselallergiemanagement opties zijn is er iets voor te zeggen dat iedere bijdrage aan een managementstrategie, zoals de introductie van hypoallergene 'novel foods' welkom is.

Dit onderzoek draagt bij aan het inzicht in de invloed van voedselallergieën op het dagelijkse leven van consumenten met een voedselallergie en laat zien dat hypoallergene 'novel foods' het dagelijkse leven van sommige voedselallergische consumenten kan verbeteren, door het gemakkelijker maken allergenen te vermijden. De resultaten van dit onderzoek bieden de voedselindustrie en wet- en regelgevers belangrijke inzichten in de mogelijkheden 'novel foods' toe te passen als allergiemanagementstrategie, waardoor zij in staat zijn beter op de behoeften van voedselallergische consumenten in te spelen.

# About the author

Margreet van Putten was born in Leidschendam, the Netherlands on April 28th 1979. She finished her secondary education in Nieuwegein at the Anna van Rijn College in 1997. After that she studied Household and Consumer studies in Wageningen at Wageningen University with a specialisation in household technology. During her university education Margreet developed an interest in combining social sciences with natural sciences. In 2001, Margreet received a Master of Science degree in Household and Consumer studies. After working for the ministry of Social Housing, Spatial Planning and Environment (VROM) and the chair of Consumer technology and product use, Margreet started as a PhD student at the Marketing and Consumer behaviour group of Wageningen University. The research focussed on the possibilities to use novel foods as part of a (food) allergy mitigation strategy. The results of this research are presented in this thesis. During the PhD research, she chaired the Mansholt Graduate School of Social Sciences PhD council and co-organised the annual PhD day. Margreet has also been involved in the MSc course Consumer behaviour, where she supervised the group work of students and provided feedback.

## Completed Training and Supervision Plan


| Description | Institute / Department | Year | ECTS* |
|---|---|---|---|
| **Courses:** | | | |
| Mansholt Introduction course | Mansholt Graduate School of Social Sciences (MG3S) | 2004 | 1,5 |
| Research Methodology, designing and conducting a PhD research project | MG3S | 2004 | 2,8 |
| Time planning and project management | WGS | 2005 | 1,2 |
| Scientific Writing | Wageningen Graduate Schools (WGS) | 2006 | 1,5 |
| Multivariate Statistiek en missing data in de praktijk | University of Utrecht, Faculty of Social Sciences | 2005 | 1,4 |
| Food Related Allergies and Intolerances | Wageningen University FCH-90306 | 2004 | 8,4 |
| Food perception and food preference | VLAG | 2005 | 1,0 |
| Nutritional and lifestyle epidemiology | VLAG | 2005 | 1,8 |
| Food risk analysis: an integrated approach combining insights from the natural and the social sciences | MG3S | 2006 | 3 |
| Quantitative Research Methodology | MG3S | 2005 | 2,5 |
| The Future Genomics Society | MG3S | 2005 | 4 |
| Qualitative Research Methodology | MG3S | 2005 | 3 |
| | | | |
| **Presentations at conferences and workshops:** | | | **3** |
| Mansholt Multidisciplinary seminar | | 2006 | 1 |
| InformAll Conference, Rome | | 2004 | 1 |
| InformAll/Europrevall Conference, Athens | | 2005 | 1 |
| **Total (minimum 30 ECTS)** | | | **35,1** |

*One ECTS on average is equivalent to 28 hours of course work